NATURAL PRODUCT STRUCTURES

BY X-RAY METHODS.

A THESIS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

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SUBMITTED BY

IAIN CAMPBELL PAUL, B.Sc.

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P R E F A C E.

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SUMMARY.

X-ray studies have been carried out on crystals of derivatives of naturally-occurring organic compounds. Three structures have been successfully determined in this way: the bitter principle, clerodin ($C_{24}H_{34}O_7$), and the mould products, byssochlamic acid ($C_{18}H_{20}O_6$) and atrovenetin ($C_{19}H_{18}O_6$).

Information on the structure of clerodin was not extensive, when crystals of a bromo-γ-lactone were provided by Professor Barton. The structure analysis was hindered by the proximity of the heavy atom to certain important structural features, which, as a consequence, proved difficult to locate. The picture of the structure, as shown by the three-dimensional Fourier maps, was clarified when it was recognised that the accepted molecular formula for clerodin was incorrect. The main remaining problem was the establishment of the correct absolute stereochemistry. The relative configuration of the molecule was found, despite some difficulties concerning the identification of the nature of the atoms in a three-membered ring, and by employing the anomalous scattering effect, the true absolute configuration of clerodin

bromolactone, and hence of clerodin itself, was established. The crystal and molecular dimensions conformed to the normal pattern, although great accuracy in the location of atomic positions was not attempted.

Professor Barton provided crystals of a p-bromophenylhydrazine derivative of the mould product byssochlamic acid. Very little was known of the structure of this compound. The major problem in this structure analysis proved to be the determination of the positions of the bromine atoms in the unit cell of the crystal. There were two bromine atoms in the asymmetric unit, and the derivative crystallised in the tetragonal system; these two facts resulted in a very complex Patterson function, which required a great deal of study before the heavy atom sites were located. Thereafter, the major problem was one of minimising the very large amount of computer time required for this complex analysis. The structure and relative stereochemistry of byssochlamic acid was established and it can be seen to occupy an important place in a series of compounds studied by Professor Barton. Some slightly anomalous molecular dimensions were found in this structure, although, once again, the limited accuracy of the analysis limits the conclusions that can be drawn.

Unlike the other two compounds, a structure had been proposed for atrovenetin, although later work had cast some doubt on its complete validity. The solution of this structure by X-ray methods proved comparatively simple, although refinement was hindered by pseudo symmetry. The structure found differed in the manner of attachment of a five-membered ring to that published. From a crystallographic view-point, this structure is interesting on account of the very close similarity of two independent molecules in the crystal. These two molecules have crystallised in a manner which bears a close resemblance to the symmetry of a higher crystal class. The molecules are prevented from crystallising in this higher class because of the presence of an asymmetric centre. Despite inaccuracies in the analysis, some interesting conclusions can be drawn regarding the molecular dimensions.

Three appendices contain an account of some work done on the crystal structures of 1:4-cyclohexanedione, dinitrogen tetroxide, and salts of furan tetracarboxylic acid. A fourth appendix contains some stereoscopic photographs of three-dimensional Fourier syntheses computed for clerodin bromolactone and atrovenetin trimethyl ether ferrichloride.

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INTRODUCTION.

Development and Application of X-ray Crystallography in Chemical Problems.

The rapid advance in the application of X-ray crystallography to elucidating the structures of naturally-occurring organic compounds in the past decade has been of the utmost importance. With the advent of the electronic digital computer, it has become simpler for the organic chemist, when confronted with an unknown structure that resists elucidation, to prepare a suitable derivative and to turn the problem over to the X-ray crystallographer. Unfortunately, in some cases, the suitability or otherwise of the derivative is not apparent for several months.

The basic techniques, which will be outlined in the following sections, have in most cases been used successfully for two-dimensional and smaller three-dimensional work prior to 1950, but only since that time has the determination of completely unknown structures containing twenty or more atoms apart from hydrogen been feasible. The pioneer work on strychnine derivatives, penicillin derivatives, and vitamin B_{12} has been followed by a very rich harvest of successful structure determinations, culminating in the elucidation of the structures of the proteins, haemoglobin and myoglobin.

The present work is of a more modest character, consisting in the elucidation of the structures of naturally-occurring organic compounds by the application of the direct heavy atom method. In two cases, the information about the structure prior to the X-ray work was meagre, while in the case of clerodin bromolactone even the accepted molecular formula proved incorrect.

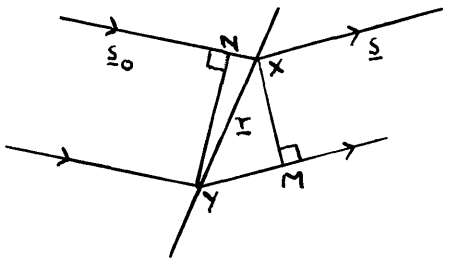
Derivation of the Laue and Bragg Equations.

From a geometric stand point, crystals consist of a three-dimensional periodic repetition of a basic geometric unit, called a unit cell. Alternatively, crystals may be considered as being made up of a large number of identical atomic arrangements repeating regularly in three-dimensions. It is convenient to replace each such group of atoms by a point, and the three-dimensional pattern of such points forms the space lattice of the crystal. In order to provide the lattice with the means to scatter radiation, it is assumed that an electron is situated at each lattice point. The positions of these electrons can be specified by a set of vectors $\underline{r}$, such that:

$$\underline{r} = m\underline{a} + n\underline{b} + o\underline{c} \quad ,$$

where $\underline{a}$, $\underline{b}$, and $\underline{c}$ are the vectors defining the unit cell of the space lattice, and m, n, and o are integers.

In (I), X and Y are two lattice points, and the direction of incident radiation is denoted by the vector $\underline{s}_o$, of length $1/\lambda$, where λ is the wavelength of the radiation. The path difference between the scattered waves from the two lattice points in a direction defined by the vector $\underline{s}$, equal in magnitude to $\underline{s}_o$, is given by:



(I)

$$YM - XN = \lambda (\underline{r}.\underline{s} - \underline{r}.\underline{s}_o) = \lambda \underline{r}.\underline{S}$$

where $\underline{S} = \underline{s} - \underline{s}_o$.

The condition for the waves to be in phase is that $\underline{r}.\underline{S}$ must be an integer, i.e. that $(m\underline{a} + n\underline{b} + o\underline{c}).\underline{S}$ must be an integer. Hence, the conditions that

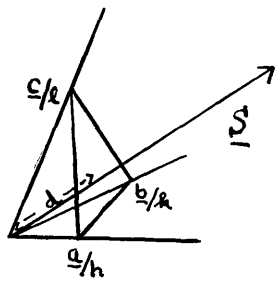
$$\underline{a}.\underline{S} = h$$
$$\underline{b}.\underline{S} = k$$
$$\underline{c}.\underline{S} = \ell$$

where h, k and ℓ are integers, must hold for a diffracted beam of maximum intensity to be produced. These conditions are known as the Laue Equations.

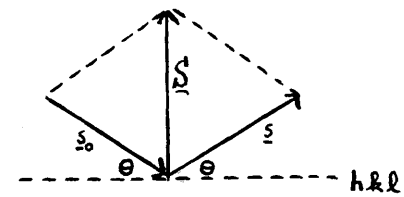
These equations may be written in the form,

$$\underline{a}/h.\underline{S} = \underline{b}/k.\underline{S} = \underline{c}/\ell.\underline{S} = 1$$

From this, it is clear that $\underline{S}$ is perpendicular to the plane defined by the intercepts, $\underline{a}/h$, $\underline{b}/k$, $\underline{c}/\ell$, i.e. the plane with Miller indices h k ℓ(II). Since,by



(II)



(III)

definition, the vector $\underline{S}$ bisects the incident and diffracted beams, and is perpendicular to the lattice plane hkℓ, a close analogy with reflexion can be drawn. The spacing d(hkℓ) of the planes is the perpendicular distance from the plane hkℓ to the origin (II) and is equal to the projection of $\underline{a}/h$, $\underline{b}/k$, and $\underline{c}/\ell$ on the vector $\underline{S}$.

$$\text{i.e.} \quad d(hk\ell) = \frac{\underline{a}/h \; \underline{S}}{|S|}$$

But, from the Laue equations, $\underline{a}/h \; \underline{S} = 1$ and

$$|S| = 2 \sin\theta/\lambda \quad \text{(III)},$$

where θ is the angle of incidence of the radiation on the lattice plane hkℓ. Hence,

$$2 d \sin\theta = \lambda$$

This is known as Bragg's Law and indicates that a 'reflexion' from a lattice plane can only take place when the angle of incidence of the X-ray beam satisfies the condition given by the equation.

The Structure Factor Expression.

A crystal with N atoms in the unit cell can be imagined to consist of N interpenetrating lattices, with all lattice points occupied by atoms. Individually, each of these lattices will obey the Laue and Bragg conditions, but, in general, the N lattices will be out of phase, so the intensities of the various planes will depend on the atomic arrangement within the unit cell.

The position of the j^{th} atom, situated at the point (x_j, y_j, z_j) where x_j, y_j, and z_j are fractions of the unit cell vectors, can be represented by $\underline{r}_j$, where

$$\underline{r}_j = x_j\underline{a} + y_j\underline{b} + z_j\underline{c}$$

The path difference between the waves scattered by the j^{th} atom and an atom at the origin of the unit cell can be shown to be $\lambda\, \underline{r}_j.\underline{S}$ and the corresponding phase difference is $2\pi\, \underline{r}_j.\underline{S}$. Combining these phase differences for all atoms in the unit cell, the expression for the complete wave scattered in the crystal would be

$$F = \sum_{j=1}^{N} f_j \exp 2\pi i \, \underline{r}_j . \underline{S}$$

$$F = \sum_{j=1}^{N} f_j \exp 2\pi i (x_j \underline{a} . \underline{S} + y_j \underline{b} . \underline{S} + z_j \underline{c} . \underline{S})$$

$$F(hk\ell) = \sum_{j=1}^{N} f_j \exp 2\pi i (hx_j + ky_j + \ell z_j)$$

In this expression, f_j represents the scattering factor of the atom, which takes account of phase differences in scattering due to the electrons within one atom. The quantity $F(hk\ell)$ is known as the structure factor and it is a complex quantity which can be represented by a modulus $|F(hk\ell)|$, known as the structure amplitude and a phase, $\alpha(hk\ell)$. The structure amplitude can be obtained from the measured intensities, but the phase is not an observable quantity.

It is often convenient to separate the real and imaginary parts of $F(hk\ell)$, so that $F(hk\ell) = A(hk\ell) + i\,B(hk\ell)$, and $\alpha(hk\ell) = \tan^{-1} \frac{B(hk\ell)}{A(hk\ell)}$, where:

$$A(hk\ell) = \sum_{j=1}^{N} f_j \cos 2\pi (hx_j + ky_j + \ell z_j)$$

and

$$B(hk\ell) = \sum_{j=1}^{N} f_j \sin 2\pi (hx_j + ky_j + \ell z_j)$$

Instead of introducing point atoms, the structure factor may be expressed in terms of the electron density at a point, $\rho(x, y, z)$; thus

$$F(hk\ell) = \int_{x=0}^{1}\int_{y=0}^{1}\int_{z=0}^{1} V\rho(x,y,z)\exp 2\pi i(hx + ky + \ell z)dx\ dy\ dz$$

Fourier Series.

As a crystal is periodic in three-dimensions, the electron density of the crystal can be represented by a Fourier series. In its most general form, a Fourier series represents a function $T(\varphi)$ as the sum of an infinite number of weighted exponentials of positive and negative values of a phase angle φ, i.e.

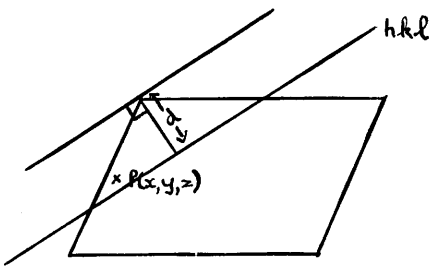
$$T(\varphi) = \sum_{n=-\infty}^{\infty} C_n \exp(i n \varphi)$$

or, alternatively,

$$T(\varphi) = \sum_{n=-\infty}^{\infty} C_n \exp(-i n \varphi)$$

The latter form is found to be the more useful in crystal structure analysis. The theory can be extended to represent a function of several variables, e.g. the electron density as a function of three co-ordinates.

As every point in space has to be covered, there should be a triply infinite number of Fourier coefficients (C_n). The periodicity of the lattice limits the number of terms to those whose direction and wavelength correspond to a particular crystal plane. A Fourier series representing the electron density as a function of x, y, and z, the fractions of the three co-ordinate axes of the unit cell, has a term for every crystal plane hkℓ.



(IV)

(IV) shows a representation of a Fourier wave hkℓ of wavelength d(hkℓ). The phase (φ) of this wave at the point P(x,y,z), where P is defined by the vector $\underline{r}$,

where $\underline{r} = x\underline{a} + y\underline{b} + z\underline{c}$

is given by $\varphi/2\pi = \underline{r}.\underline{S}$. Hence,

$$\varphi = 2\pi(hx + ky + \ell z)$$

The electron density in a crystal can therefore be represented by a triple Fourier series of the type,

$$\rho(x\ y\ z) = \sum_{h}\sum_{k}\sum_{\ell}^{-\infty\ \infty} C_n \exp - 2\pi i(hx + ky + \ell z)$$

The structure factor $F(h'k'\ell')$ of a set of reflexions $(h'k'\ell')$ is given by:

$$F(h'k'\ell') = \int_0^1\int_0^1\int_0^1 V\rho(xyz)\ \exp 2\pi i(h'x + k'y + \ell' z)\,dx\,dy\,dz$$

Substituting for $\rho(xyz)$,

$$F(h'k'\ell') = \int_0^1\int_0^1\int_0^1 \sum_{h}\sum_{k}\sum_{\ell}^{+\infty}_{-\infty} C_n \exp 2\pi i\left[(h'-h)x + (k'-k)y + (\ell'-\ell)z\right] V\,dx\,dy\,dz$$

The integral of a sum of terms is the sum of the individual integrals, therefore

$$F(h'k'\ell') = \sum_{h}\sum_{k}\sum_{\ell}^{+\infty}_{-\infty} \int_0^1\int_0^1\int_0^1 C_n \exp 2\pi i\left[(h'-h)x + (k'-k)y + (\ell'-\ell)z\right] V\,dx\,dy\,dz$$

Each of these individual integrals vanishes, unless $h' = h$, $k' = k$ and $\ell' = \ell$, when

$$F(hk\ell) = V\,C_n\,(hk\ell)$$

The expression for the electron density of the crystal $\rho(xyz)$ takes the form:

$$\rho(xyz) = \frac{1}{V}\sum_{h}\sum_{k}\sum_{\ell}^{+\infty}_{-\infty} F(hk\ell)\exp -2\pi i(hx + ky + \ell z)$$

The Phase Problem and the Heavy Atom Method.

As demonstrated in the last section, the electron density in a crystal can be evaluated by Fourier methods provided the structure factors are known. Unfortunately, only the structure amplitudes can be determined by measurement, leaving the relative phases unknown. The determination of these phases constitutes the basic problem of X-ray structure analysis, and for a specific crystal structure, no general method for finding the phases exists.

When dealing with the structures of large organic molecules containing from twenty to sixty atoms other than hydrogen, the 'heavy atom' method has been found to be a powerful approach to the problem (Robertson and Woodward, 1940). If it is possible to prepare a derivative containing one or two atoms with an atomic number much greater than that of the remainder of the atoms, and to locate the position of this atom within the unit cell (x_A, y_A, z_A), then the structure can often be solved. The heavy atom contribution to the relative phases dominates the contribution of the other atoms and the phase $\alpha_A(hk\ell)$, due to the heavy atom alone, found from the equation:

$$\alpha_A(hk\ell) = \tan^{-1} B/A = \tan^{-1}\left[\frac{\sin 2\pi(hx_A + ky_A + \ell z_A)}{\cos 2\pi(hx_A + ky_A + \ell z_A)}\right]$$

is a close approximation to the true phase $\alpha(hk\ell)$.

Consequently, a Fourier series can be evaluated with the measured structure amplitudes and the phases $\alpha_A(hk\ell)$, with a good chance that it will provide a reasonable and recognisable approximation to the actual electron density. If genuine fragments of the structure can be identified from this electron density map, these atoms may also be employed in a phasing calculation and a closer approximation to the true phases should be obtained.

The effectiveness of a heavy atom in determining the phases in a particular structure can be roughly indicated by the ratio of the square of the atomic number of the heavy atom to the sum of the squares of the atomic numbers of the light atoms. This ratio should be about unity for maximum effectiveness (Lipson and Cochran, 1953). Sim(1957) has done further calculations on the number of phases that should be determined within acceptable limits for various ratios of scattering factors of heavy and light atoms. It is undesirable for the atom to be so heavy that the square of the atomic number is very much greater than the sum of the squares of the atomic numbers of the other atoms. This could lead to undesirable effects, such as diffraction 'ripples', which might obliterate genuine detail or cause it to be displaced from its true position, or could cause errors in the measured structure amplitudes due to high absorption of the X-rays.

Vector Methods.

In the preceding section, it was shown that in certain circumstances, the phase problem could be overcome provided the position of a heavy atom could be found within the unit cell. Patterson (1934) defined a quantity:

$$P(uvw) = \int_0^1 \int_0^1 \int_0^1 \rho(xyz)\,\rho(x+u,\ y+v,\ z+w)\,dx\,dy\,dz$$

In this expression, $\rho(x+u,\ y+v,\ z+w)$ is the distribution of scattering material about (xyz) as a function of u, v, and w and it represents a distribution similar to $\rho(xyz)$ but displaced from (xyz) by the parameters u, v and w. The function P(uvw) will have a large value when both $\rho(x,y,z)$ and $\rho(x+u,\ y+v,\ z+w)$ are large, i.e. when atoms are situated at (x, y, z) and (x+u, y+v, z+w). The function gives a representation of all the interatomic vectors in the unit cell. The heavier the atoms at the points (x, y, z) and (x+u, y+v, z+w), the greater will be the value of P(u, v, w).

The great importance of the Patterson function becomes apparent when the Fourier expressions for the electron density are substituted in the above equation.

$$P(u,v,w) = {}^{1}/_{V}2 \sum_{h}\sum_{k}\sum_{\ell=-\infty}^{+\infty}\sum_{h'}\sum_{k'}\sum_{\ell'} \int_0^1\int_0^1\int_0^1 F(hk\ell)\exp\{-2\pi i(hx+ky+\ell z)\}$$

$$F(h'k'\ell')\exp\{-2\pi i(h'x + k'y + \ell' z)\}\exp\{-2\pi i(h'u + k'v + \ell' w)\}\, dx\, dy\, dz$$

This expression vanishes unless, $h = -h'$, $k = -k'$ and $\ell = -\ell'$, when

$$P(u,v,w) = {}^{1}/_{V}2 \sum_{-\infty}^{+\infty}\sum\sum F(hk\ell)\, F(\bar{h}\bar{k}\bar{\ell})\exp\{-2\pi i(h'u + k'v + \ell' w)\}$$

and, as $F(hk\ell)$ and $F(\bar{h}\bar{k}\bar{\ell})$ are complex conjugates,

$$P(u\,v\,w) = {}^{1}/_{V}2 \sum_{0}^{\infty}\sum_{-\infty}^{\infty}\sum_{-\infty}^{\infty} |F(hk\ell)|^2 \cos 2\pi(hu + kv + \ell w)$$

It can be seen that the Patterson synthesis may be evaluated from a knowledge of the structure amplitudes alone. The position of a heavy atom in the unit cell can often be found by this method and this provides the starting point in the solution of the phase problem.

Harker (1936) has shown that, owing to the symmetry of the crystal, special concentrations of vectors are found in certain planes and lines of the Patterson function. For example, in the space group $P2_1$, a planar concentration of vectors is found on the section $P(u, \frac{1}{2}, w)$.

The Relation between the Intensity and Structure Amplitude.

If E is the total energy reflected by the volume dV in the course of a single passage of the crystal through the region of a Bragg reflexion, it can be shown (e.g. Buerger, 1960) that:

$$E = \left(\frac{I_o \lambda^3 N^2 dV}{\omega}\right)\left(\frac{e^4}{m^2 c^4}\right)\left(\frac{1 + \cos^2 2\theta}{2}\right) L |F|^2$$

where,

I_o = the intensity of the radiation striking the crystal

λ = the wavelength of the radiation

N = the number of unit cells/unit volume

dV = the volume of the crystal

ω = the rate of rotation of the crystal

e = the electronic charge

m = the mass of the electron

c = the velocity of light

θ = the Bragg angle

$|F|$ = the structure amplitude

L = the Lorentz factor.

This formula is based on the assumption of a very small crystal, much smaller in fact than the size normally used. That the formula is applicable to the normal size of crystals is due to imperfections that result in the crystal being made up of a mosaic of very small blocks.

The factor $\left(e^4/m^2c^4\right)$ is introduced as it occurs in the expression for scattering due to a single electron. The term $\left(1 + \cos^2 2\theta/2\right)$ is known as the polarisation factor and accounts for the incident X-ray beam being unpolarised with respect to the plane of 'reflexion'. It is independent of the geometric arrangement for recording intensities. The factor L, known as the Lorentz factor, equals $1/\sin 2\theta$ when the rotation of the crystal is about an axis perpendicular to the X-ray beam, but other corrections may have to be applied if a more complex motion of the crystal relative to the X-ray beam is employed.

In addition to these corrections, the effects of primary and secondary extinction and absorption may be important. Primary extinction is caused by 'reflexion' of the incident X-ray beam from the surface layers of the crystals, while secondary extinction is due to the 'screening' of the lower blocks of the mosaic structure by the outer blocks from the incident beam.

Refinement:

(a) By Fourier Methods.

When a structure has been solved, a process of refinement has still to be followed to obtain good agreement between observed and calculated structure amplitudes, and to approximate the calculated phases to the true phases.

This can be done initially using $F_{obs.}$ Fourier syntheses, and the new atomic positions obtained from these syntheses can then be used in a further round of structure factor calculations. This method, however, could only give the structure with great accuracy under certain conditions. A Fourier series can only legitimately be applied to a crystal structure analysis when an infinite number of terms are available; hence, using X-rays of wavelength about 1.5 Å places a severe limitation on the amount of data that can be collected. It is quite reasonable to expect that for any postulated structure, there will be structure factors outwith the recording limit of the radiation having quite large amplitudes. The omission of such terms from the observed data causes termination of series effects.

These effects are shown as diffraction ripples near the atoms in the structure, and are in effect a series of troughs and waves emanating from the positions of the atomic centres. These disturbances will influence the position of the neighbouring atoms and cause shifts from the true positions. Allowance for this effect can be made by a method due to Booth (1946).

The final $F_{obs.}$ synthesis, calculated from a model containing all the atoms in the structure, is known to have the peaks displaced by unknown amounts due to termination of series effects. Another Fourier series, with the same phases, but with $F_{calc.}$ as coefficients can be computed. If there were no errors due to termination of series effects, the position of the peaks in the $F_{calc.}$ map should be identical with the sites proposed in the model. Hence, the deviations of the peaks from those sites (Δx, Δy, Δz) represent the correction, with change of sign, to be applied to the positions of the peaks in the $F_{obs.}$ map. This correction is known as the 'back-shift' correction. It is based on the assumption that no errors exist in the postulated structure, except those due to termination of series effects, and hence should not be applied until the refinement with F_o syntheses has reached its limit of effectiveness.

(b) <u>By Least Squares Procedures</u>.

The quantity $\sum w\Delta^2$, where $\Delta = |F_o(hk\ell)| - |F_c(hk\ell)|$, can be minimised with respect to the structure parameters used in calculating F_c. The summations are over a set of independently observed planes, which are allotted weights according to the estimated accuracy of the observations.

If $u_1, u_2, \ldots u_j, \ldots u_n$ are the n parameters on which F_c is dependent, then the condition for $\sum w\Delta^2$ to be a minimum is:

$$\frac{\partial \sum w\Delta^2}{\partial u_j} = 0$$

$$\text{i.e.} \quad \sum w\Delta(hk\ell)\frac{\partial \Delta(hk\ell)}{\partial u_j} = 0$$

The normal equations for the corrections, ε_j, to the trial set of parameters, u_j, are the n simultaneous linear equations,

$$\sum_{i=1}^{n} \varepsilon_i \left\{ \sum w(hk\ell)\frac{\partial \Delta(hk\ell)}{\partial u_j} \cdot \frac{\partial \Delta(hk\ell)}{\partial u_i} \right\}$$

$$= -\sum w(hk\ell)\Delta(hk\ell)\frac{\partial \Delta(hk\ell)}{\partial u_j}$$

for $j = 1, 2, \ldots . n$

$\frac{\partial \Delta(hk\ell)}{\partial u_j}$ being evaluated for the trial set of parameter values. The off-diagonal coefficients, $\sum w\left(\frac{\partial \Delta}{\partial u_j}\right)\left(\frac{\partial \Delta}{\partial u_i}\right)$, of ε_i in the normal equations are often omitted in the refinement, in which case the atomic parameters and the thermal parameters are treated separately.

In the least-squares program written by Dr.J.S.Rollet,

the atomic positional parameters are evaluated from a 3 x 3 matrix for each atomic position, the thermal vibrational parameters are evaluated from a 6 x 6 matrix for each atom, and the scale factor is evaluated from a 2 x 2 matrix with the parameter Q representing the overall vibrational parameter, such that $\frac{\partial |F_o|}{\partial Q} = - F_c \sin^2 \theta$

Cruickshank (1952) considers that for structures with a large collection of three-dimensional data, these limitations are valid except in the case of co-ordinate interactions between two atoms, one of which dominates the phase determination.

The standard deviations of the quantities u_j can be found from the totals, $\sum w \frac{\partial \Delta}{\partial u_j} \cdot \frac{\partial \Delta}{\partial u_j}$

$$\text{i.e. } \sigma(u_j)^2 = \frac{\sum w \Delta^2}{(N - S) \sum w \frac{\partial \Delta}{\partial u_j} \cdot \frac{\partial \Delta}{\partial u_j}}$$

where N is the number of independent observations,

and S is the number of parameters to be refined.

Anomalous Scattering and the Distinction of Entantiomorphs by X-rays.

The structure factor $F(hk\ell)$ can be written as

$$F(hk\ell) = \sum_{j=1}^{N} f_j \exp 2\pi i \, \underline{r}_j . \underline{S}$$

On inversion of $\underline{r}_j$, the structure changes to its enantiomorph, and $F(hk\ell)$ takes its conjugate value $F(hk\ell)^*$, while the intensity, $I(hk\ell) = F(hk\ell).F(hk\ell)^*$, remains unchanged. The only circumstance that could invalidate this condition would be for one of the scattering factors to be complex. In such a case, the intensity of a reflexion would change on inversion of the structure. If the scattering factor f_j is represented by $f'_j\, e^{i\delta_j}$, then the structure factor $F(hk\ell)$ becomes:

$$F(hk\ell) = \sum_{j=1}^{N} f'_j \exp\left[i\,\delta_j + 2\pi i(\underline{r}_j.\underline{S})\right]$$

On inversion of the structure, the intensities could only remain the same if all the δ_j values were equal.

A complex scattering factor occurs when the phase change in the scattering process differs from the corresponding phase change in the scattering by a free electron so long as the difference, $\delta \neq \pi$. In the expression for the structure factor it is necessary to ensure that the terms due to anomalous scattering and normal scattering have the correct sign relative to each other. Consequently, great care must be taken to ensure that the photographs are indexed correctly and that the structure factor calculations are based on this indexing.

For non-centrosymmetric crystals, the sequence of atoms from the side $hk\ell$ is the reverse of that on the side

$\overline{hk\ell}$. This allows the distinction between enantiomorphs to be made by measurement of reflexions from the same crystal instead of equivalent reflexions from crystals of each enantiomorph having to be compared.

The complex scattering factor $f e^{i\delta}$ may be written:

$$f e^{i\delta} = f^{o} + \Delta f' + i\Delta f'' ,$$

where $\Delta f'$ and $\Delta f''$ have been calculated on the basis of Hönl's theory (James, 1948) and values of $\Delta f'$ and $\Delta f''$ for various exciting radiations have been listed by Dauben and Templeton (1955).

PART I.

The Structure of Clerodin.

X-ray Analysis of Clerodin Bromolactone.

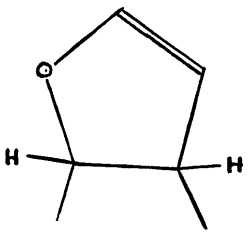
The Structure of Clerodin: X-ray Analysis of Clerodin Bromolactone.

Introduction:

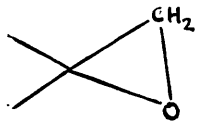
Clerodin is the bitter principle of *Clerodendron Infortunatum* or the Indian Bhat or Bhant, a gregarious shrub, common in the warm regions of India from Gurhwal and Assam to Ceylon. Indians used the plant as a vermifuge, an anthelmintic and as an effective and cheap substitute for *Chiretta*.

Banerjee (1937) investigated the plant in order to find the principle responsible for the therapeutic action. He succeeded in extracting and isolating colourless, needlelike crystals of an extremely bitter substance which he named clerodin and showed to be the active agent in the Bhant. Banerjee assigned clerodin the molecular formula $C_{13}H_{18}O_3$, but was unable to obtain much information about its structure. Chaudhury and Dutta (1951, 1954) arrived at the molecular formula $C_{28}H_{40}O_8$ for clerodin and carried out investigations on the nature of the oxygen atoms in the molecule. They succeeded in characterising an acetate grouping ($-O.CO.CH_3$) and thought that there were four hydroxyl groups present.

Barton (1960) had evidence that a vinyl ether grouping (I), two acetate groups, and an epoxide ring (II)



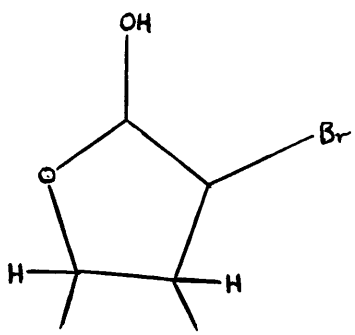
(I)



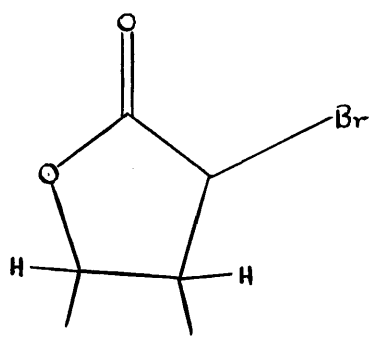
(II)

were present in clerodin. He had also shown that analytical results were consistent with a formula of $C_{21}H_{30}O_6$ for clerodin. By addition of hypobromous acid to the vinyl ether grouping (I), Barton was able to prepare a bromohydrin (III), which on oxidation gave a bromo-γ-lactone (IV).

The X-ray work was carried out mainly on clerodin bromolactone, although some preliminary measurements were made on clerodin bromohydrin, crystals of both compounds being supplied by Professor Barton.



(III)



(IV)

Experimental:

Crystal Data.

Clerodin Bromohydrin; ($C_{24}H_{35}O_8Br$); M = 530.9; m.p. 186-187°(decomp.); $d_{(calc.)}$ = 1.409, $d_{(found)}$ = 1.429 (by flotation); Orthorhombic, a = 11.44 ± 0.03, b = 9.73 ± 0.06, c = 22.52 ± 0.15 Å. V = 2504.5 Å^3. No. of mols. (Z) = 4. Absent spectra, (hOO) when h is odd, (OkO) when k is odd, (OOℓ) when ℓ is odd. Space group $P2_12_12_1$ (D_2^4). Absorption Coefficient for X-rays (λ = 1.542 Å) μ = 28.4 cm.$^{-1}$ Total number of electrons per unit cell = F(000) = 1112.

Clerodin Bromolactone; ($C_{24}H_{33}O_8Br$); M = 528.9; m.p. 168-169°. $d_{(calc.)}$ = 1.442, $d_{(found)}$ = 1.432 (by flotation); Orthorhombic, a = 10.55 ± 0.03, b = 10.12 ± 0.03, c = 22.82 ± 0.07 Å; V = 2436.4 Å^3; No. of molecules/cell (Z) = 4. Absent spectra, (hOO) when h is odd, (OkO) when k is odd, (OOℓ) when ℓ is odd. Space group, $P2_12_12_1$ (D_2^4). Absorption Coefficient for X-rays (λ = 1.542 Å) μ = 28.4 cm.$^{-1}$ Total number of electrons per unit cell = F(000) = 1104.

Preliminary measurements were carried out on both clerodin bromohydrin and clerodin bromolactone. The two

compounds belonged to the same space group and had cell dimensions of a similar order of magnitude. The crystals of the bromolactone were better formed than those of the bromohydrin and gave sharper 'reflexions'. The data for the bromolactone went out to a greater limit than the data for the bromohydrin. Consequently the X-ray analysis was carried out on clerodin bromolactone.

Rotation, oscillation, Weissenberg and precession photographs were taken with CuK_α radiation ($\lambda = 1.542$ Å), and Molybdenum K_α ($\lambda = 0.7107$ Å) radiation. The cell dimensions were obtained from rotation and precession photographs. Small crystals of approximately square cross-section were used to collect the intensities on zero-layer and equi-inclination Weissenberg photographs. Two series of photographs were taken from crystals rotated about the a- and b- axes. The intensities were estimated visually, using the multiple film technique (Robertson, 1943) and a calibrated step-wedge. The intensities were corrected for Lorentz, polarisation and rotation factors for upper layers and the values of the structure amplitudes (F_o) were obtained from the mosaic crystal formula. The various zones were placed on the same relative scale by reference to common reflexions from

both series of photographs. At a later stage in the analysis, the structure amplitudes were placed on the correct absolute scale by comparison with the calculated values $|F_c|$. In all 1512 independent structure factors were obtained.

Structure Determination.

I. The Determination of the Heavy Atom Positions.

It was hoped to determine the positions of the bromine atoms in the unit cell by selecting the concentrations of vector peaks due to Br - Br vectors from either the two-dimensional Patterson projections or from the full three-dimensional Patterson synthesis. For a crystal belonging to the orthorhombic system, the expression for the Patterson function P(UVW) is:

$$P(UVW) = {}^{8}/_{V_c} \sum_{0}^{\infty} \sum_{0}^{\infty} \sum_{0}^{\infty} |F(hk\ell)|^2 \cos 2\pi hU \cos 2\pi kV \cos 2\pi \ell W$$

This expression can be simply reduced to that for the Patterson projections P(UW) and P(VW) down the b- and a- axes respectively. Prior to computation of any of these functions the coefficients of the series $|F(hk\ell)|^2$ were modified to $|F(hk\ell)|^2 M(\underline{S})$ where

$$M(\underline{S}) = \left\{ \hat{f}_o \exp (\sin^2\Theta/\lambda^2) \right\}^{-2}.$$

The vectors to be expected between bromine atoms in the space group $P2_12_12_1$ with one molecule in the asymmetric unit are shown in Table I.

The two-dimensional Patterson projections (VW) and (UW) were computed using 205 and 218 terms respectively; the maps are shown in Figs. I and II. In the part of

TABLE I.

Vectors to be expected with one bromine atom per equivalent position in the space group $P2_12_12_1$.

-	$\frac{1}{2}+2x_{Br}, 2y_{Br}, \frac{1}{2}$	$\frac{1}{2}, \frac{1}{2}+2y_{Br}, 2z_{Br}$	$2x_{Br}, \frac{1}{2}, \frac{1}{2}+2z_{Br}$
$\frac{1}{2}-2x_{Br}, -2y_{Br}, \frac{1}{2}$	-	$-2x_{Br}, \frac{1}{2}, \frac{1}{2}+2z_{Br}$	$\frac{1}{2}, \frac{1}{2}-2y_{Br}, 2z_{Br}$
$\frac{1}{2}, \frac{1}{2}-2y_{Br}, -2z_{Br}$	$2x_{Br}, \frac{1}{2}, \frac{1}{2}-2z_{Br}$	-	$\frac{1}{2}+2x_{Br}, -2y_{Br}, \frac{1}{2}$
$-2x_{Br}, \frac{1}{2}, \frac{1}{2}-2z_{Br}$	$\frac{1}{2}, \frac{1}{2}+2y_{Br}, -2z_{Br}$	$\frac{1}{2}-2x_{Br}, 2y_{Br}, \frac{1}{2}$	-

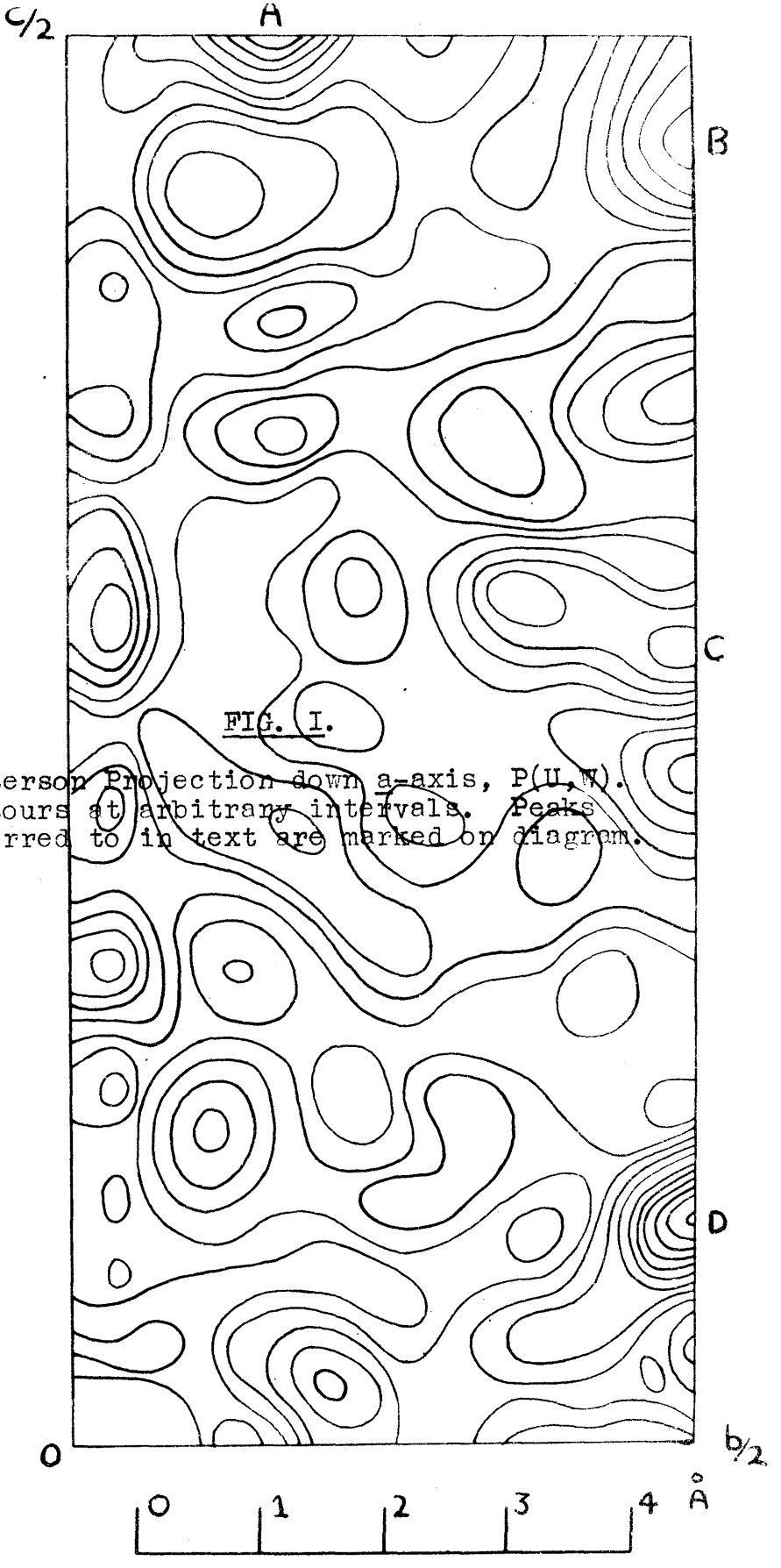
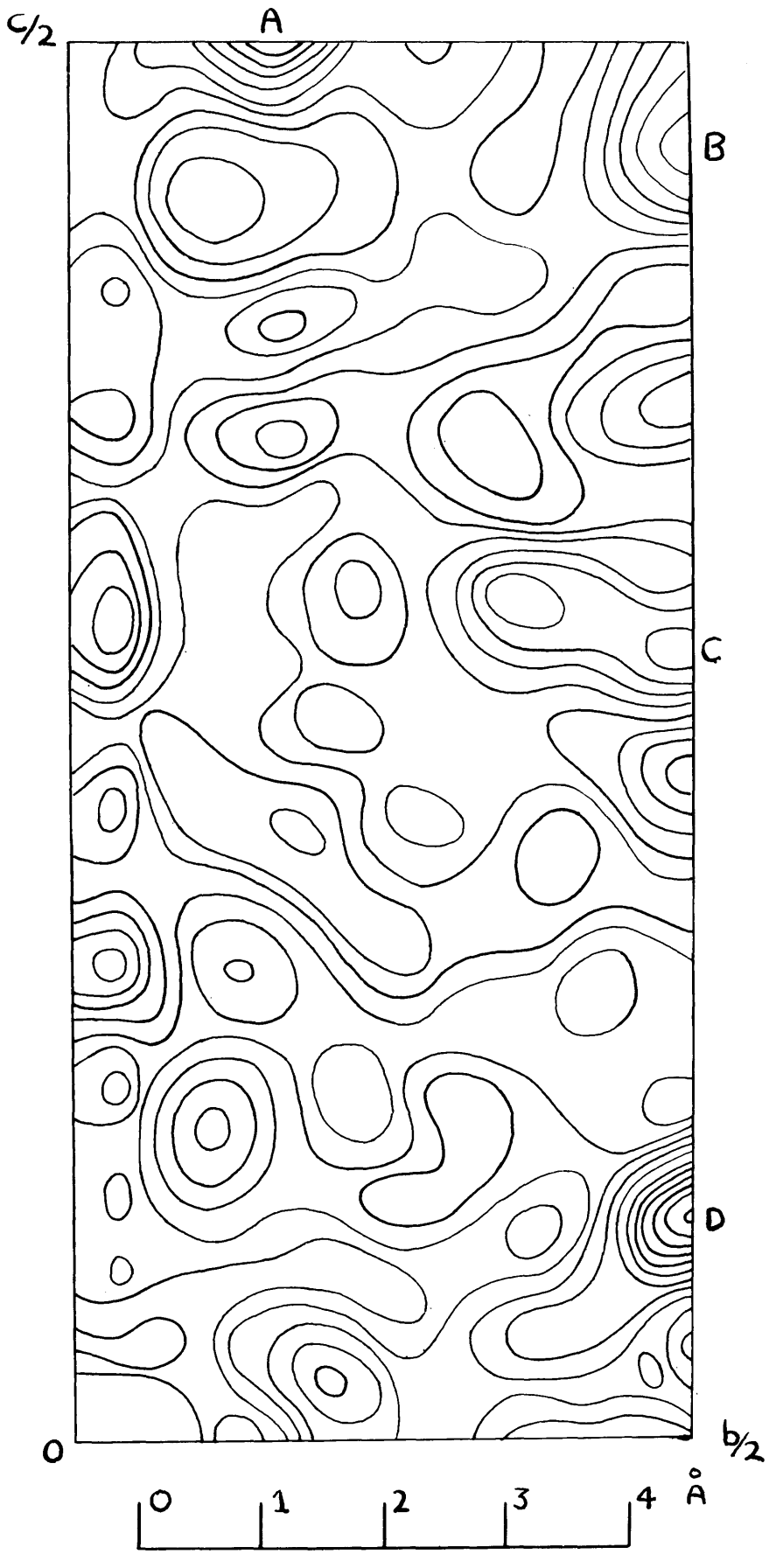


FIG. I.

Patterson Projection down a-axis, P(U,W). Contours at arbitrary intervals. Peaks referred to in text are marked on diagram.


c/2
A
B
C
D
0
b/2
0
1
2
3
4
Å

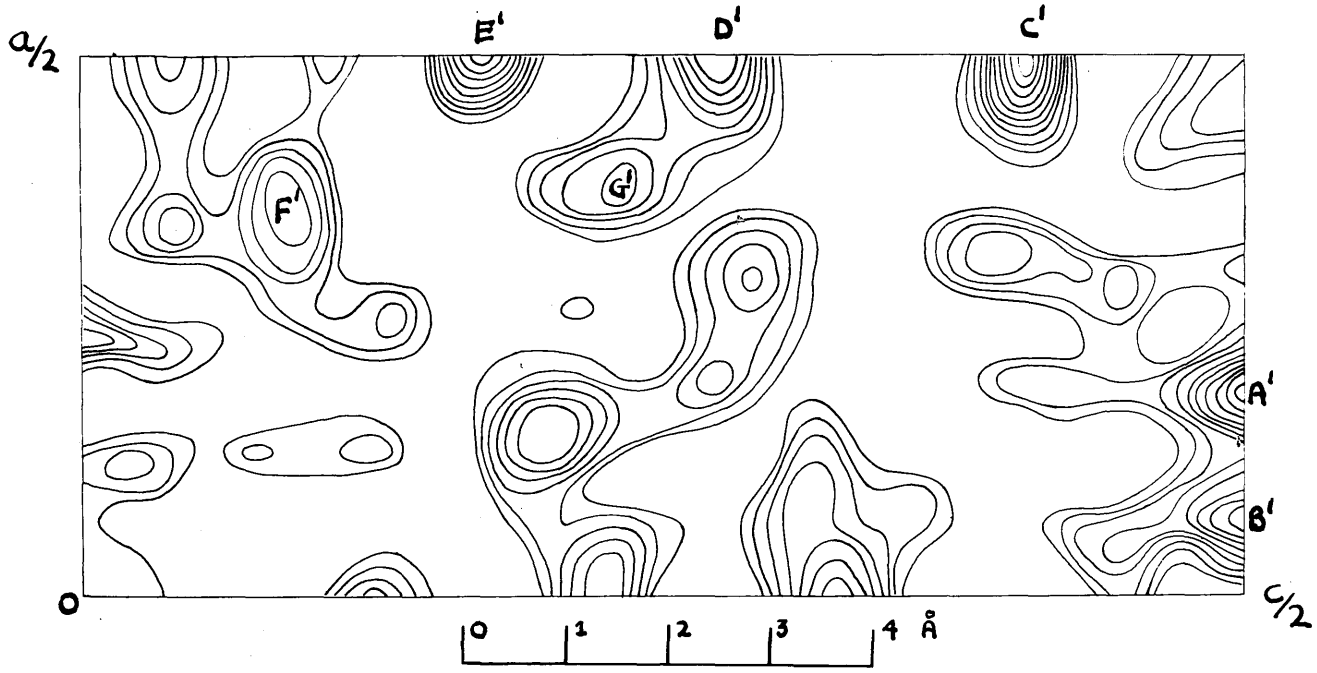


Fig.II. Patterson Projection down b-axis, P(U,W). Contours at arbitrary intervals. Peaks referred to in text are marked on diagram.

the (VW) projection shown there should be double weight peaks at $2y_{Br},\frac{1}{2}$ on the line, $(V,\frac{1}{2})$ and at $\frac{1}{2},\frac{1}{2}-2z_{Br}$ on the line $(\frac{1}{2},W)$, with a single weight peak at $\frac{1}{2}-2y_{Br}$, $2z_{Br}$ in a general position. The concentration of vectors at $2y_{Br},\frac{1}{2}$ is clearly peak A; for the concentration of vectors on the line $(\frac{1}{2},W)$ there are several possibilities which cannot be distinguished by the presence of any heavy concentration of vectors in a general position.

In the part of the (UW) Patterson projection shown in Fig.II, there should be peaks of double weight at $\frac{1}{2}-2x_{Br}$, $\frac{1}{2}$ on the line $(U,\frac{1}{2})$ and at $\frac{1}{2},2z_{Br}$ on the line $(\frac{1}{2},W)$, with a single weight peak at $2x_{Br}$, $\frac{1}{2}-2z_{Br}$ in a general position. The presence in a general position of peak F' which could be the concentration of vectors at $2x_{Br},\frac{1}{2}-2z_{Br}$ would indicate that the two other concentrations are the peaks A' and C', the latter peak corresponding to the peak D on Fig.I. In this way a consistent set of bromine co-ordinates can be obtained from the two Patterson projections. Unfortunately, at least one other set could be obtained. On the projection (UW) there is a peak G' which could be the general peak corresponding to D' along the line $(\frac{1}{2},W)$, which would be consistent with the occurrence of peak C on the projection (VW) along the line $(\frac{1}{2},W)$. Although the first set is made up of stronger vector concentrations,

it was thought desirable to compute the three Harker sections of the three-dimensional Patterson synthesis at $(\frac{1}{2},V,W)$, $(U,\frac{1}{2},W)$ and $(U,V,\frac{1}{2})$.

These sections are shown in Figs. III, IV and V and should contain respectively vector concentrations at $\frac{1}{2}-2y_{Br}$, $2z_{Br}$; $2x$, $\frac{1}{2}-2z_{Br}$; and $\frac{1}{2}-2x_{Br}$, $2y_{Br}$. The largest peak on each section gave a consistentset of values for x_{Br}, y_{Br}, and z_{Br} which corresponded to the first set obtained from the two-dimensional Patterson projections.

The co-ordinates obtained for the bromine atom in this way were:

$$x/a = 0.144; \quad y/b = 0.087; \quad z/c = 0.204.$$

These co-ordinates, being in quite general positions, should give satisfactory phase determination of the structure factors.

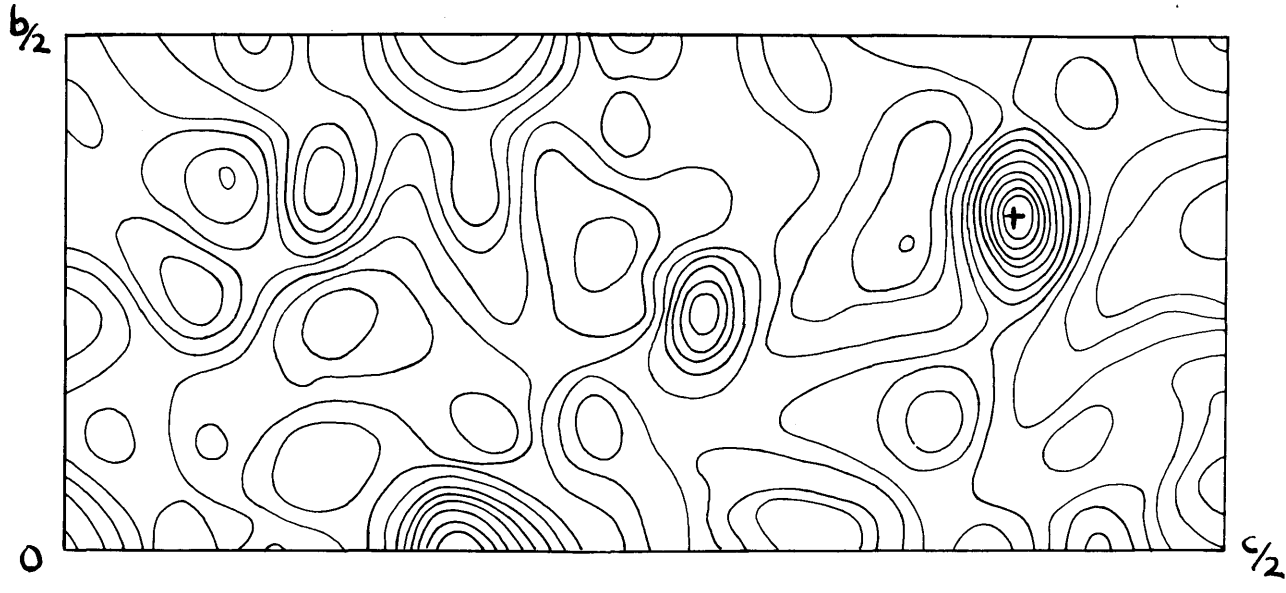


Fig.III. Three-dimensional Sharpened Patterson Synthesis. Section P($\frac{1}{2}$,V,W). Contours at arbitrary intervals. Br-Br vector marked.

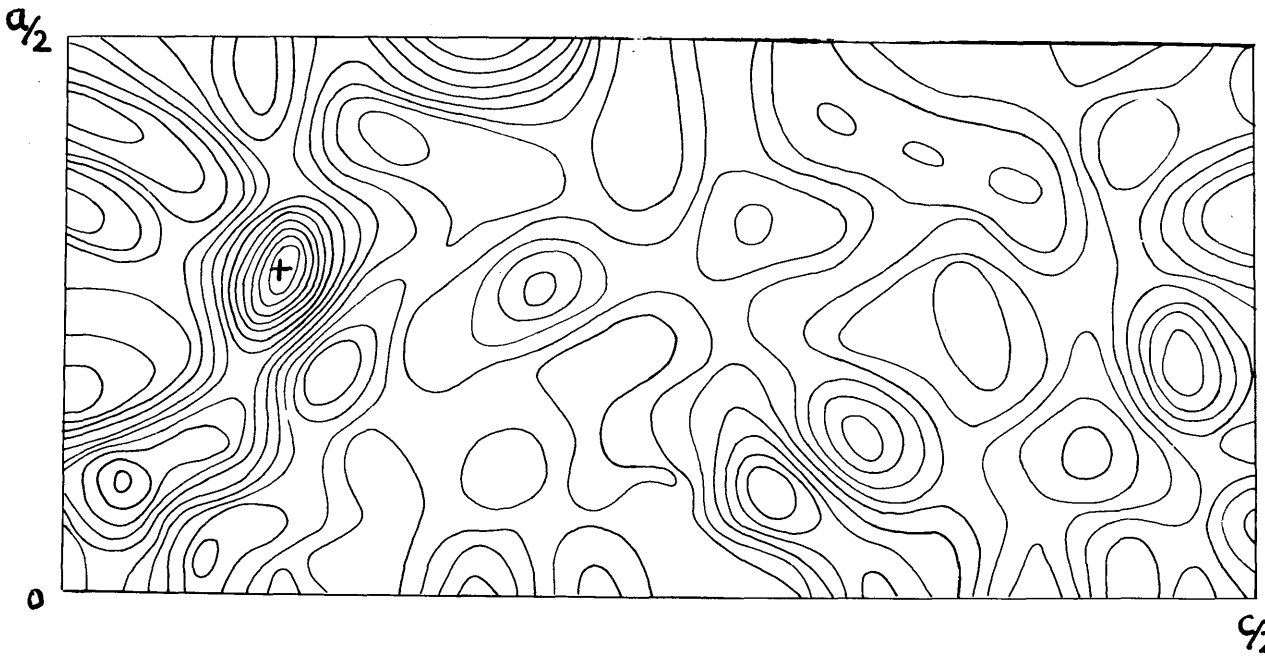


Fig.IV. Three-dimensional Sharpened Patterson Synthesis. Section P(U,$\frac{1}{2}$,W). Contours at arbitrary intervals. Br-Br vector is marked.

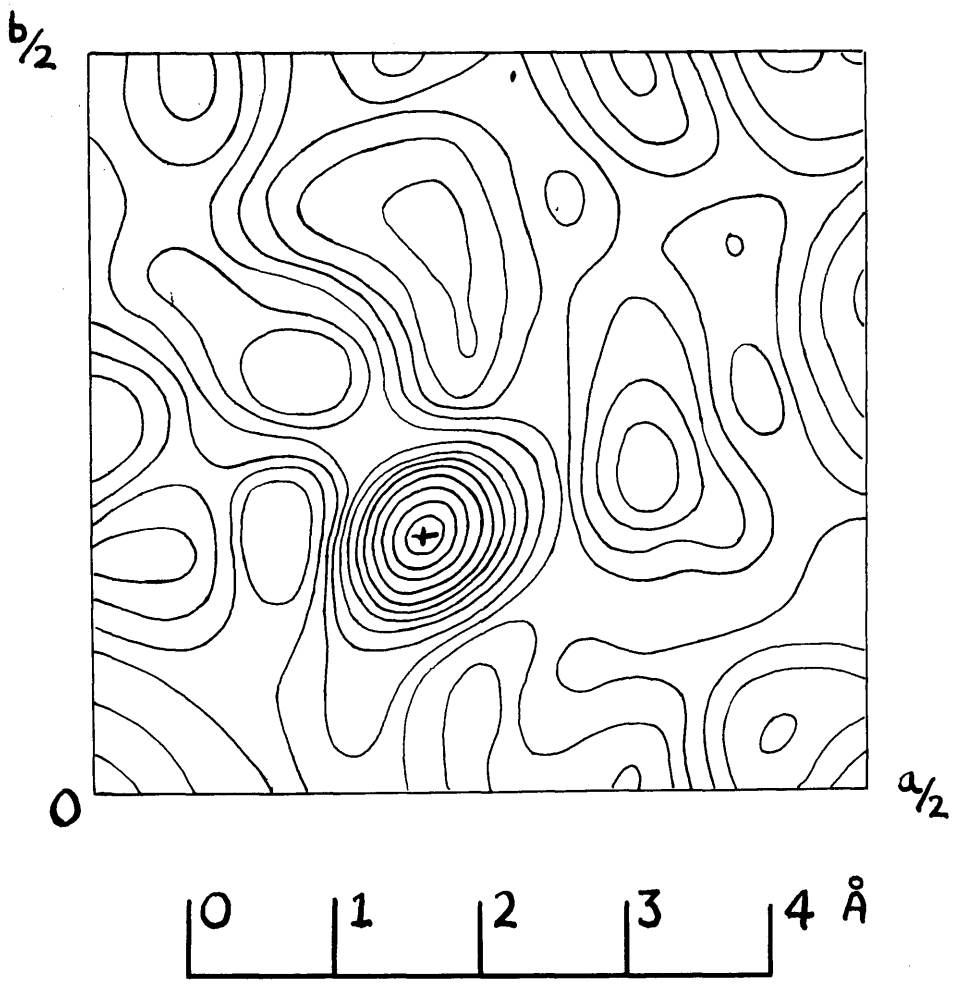


Fig.V. Three-dimensional Sharpened Patterson Synthesis. Section P(U,V,$\frac{1}{2}$). Contours at arbitrary intervals. Br-Br vector is marked.

TABLE II.

The Course of the Analysis.

2-D Patterson Projections

3-D Patterson Synthesis (Harker Sect$^{n.}$)

↓ Br co-ordinates B_{θ} = 3

Structure Factor I R = 51%

Fourier Map I computed with 1426 terms

3-D Super position Map

↓ 15 atoms + Br B_{θ} = 3

Structure Factor II R = 43%

Fourier Map II 1443 terms

↓ 14 atoms + Br B_{θ} = 3

Structure Factor III R = 42%

Fourier Map III 1466 terms

↓ 21 atoms + Br (B_{θ} = 3)

→ 2-Dimensional S.F. calcul$^{n.}$ Fourier Projection

Structure Factor IV R = 40%

Fourier Map IV 1414 terms

Solution of Structure apart from config$^{n.}$ of C_{20}

↓ 31 atoms (B_{θ} = 3) + Br

Structure Factor V R = 32%

Fourier V 1494 terms

↓ 32 atoms (5 as Oxygen) + Br B_{θ} = 3

- Cont'd -

TABLE II. (Cont'd)

The Course of the Analysis.

Structure Factor VI R = 30%

Fourier VI All terms.

↓ 32 atoms (7 as Oxygen) + Br (B_θ = 3)

Structure Factor VII R = 29%

Fourier VII ($F_o + F_c$)

↓ 32 atoms (7 as Oxygen) + Br (B_θ = 4)

Structure Factor VIII R = 24%

Fourier VIII ($F_o + F_c$)

↓ 32 atoms (7 as Oxygen) (B_θ = 4)

Structure Factor IX R = 22.5%

Fourier IX ($F_o + F_c$)

↓ 32 atoms (7 as Oxygen) (B_θ = 4)

Structure Factor X R = 21.4%

Fourier X ($F_o + F_c$)

↓ 32 atoms (8 as Oxygen) B_θ assigned on basis of $F_o + F_c$ synthesis.

Least Squares I R = 20.8%

Solve I $\Sigma w\Delta^2 = 1572$

↓ Br anisotropic, all others isotropic B_θ

Least Squares II R = 19.3%

Solve II $\Sigma w\Delta^2 = 1005$

↓ Br + O atoms anisotropic
C atoms isotropic

- Cont'd -

TABLE II. (Cont'd)

The Course of the Analysis

Least Squares III R = 18.0%

Solve III $\Sigma w \Delta^2 = 872$

↓ All atoms anisotropic

Least Squares IV R = 17.2%

Solve IV $\Sigma w \Delta^2 = 1240$ (Using different weighting system)

↓

Final S.F. Calculation (All atoms anisotropic)

Final F_o map R = 16%.

II. The First Cycle of Structure Factor and Fourier Calculations.

The ratio $\Sigma f_H^2 / \Sigma f_L^2$ has a value of 0.870 for the clerodin bromolactone structure. A flow diagram of the course of the structure analysis is given in Table II.

The first structure factor calculation was carried out on the positions of the bromine atoms found from the three-dimensional Patterson. The expression for structure factors in the space group $P2_12_12_1$ is:

when $h + k = 2n$, $A = 4 \cos 2\pi hx \cos 2\pi ky \cos 2\pi \ell z$

$B = -4 \sin 2\pi hx \sin 2\pi ky \sin 2\pi \ell z$

and when $h + k = 2n + 1$,

$A = -4 \sin 2\pi hx \sin 2\pi ky \cos 2\pi \ell z$

$B = 4 \cos 2\pi hx \cos 2\pi ky \sin 2\pi \ell z$

This calculation showed a discrepancy, $R = \frac{\Sigma ||F_o| - |F_c||}{\Sigma F_c}$, of 51%. The values of F_o and F_c were examined and in the cases where $|F_o| > 2|F_c|$, the reflexion was omitted from the first Fourier series. The expression for the electron density in the space group $P2_12_12_1$ is

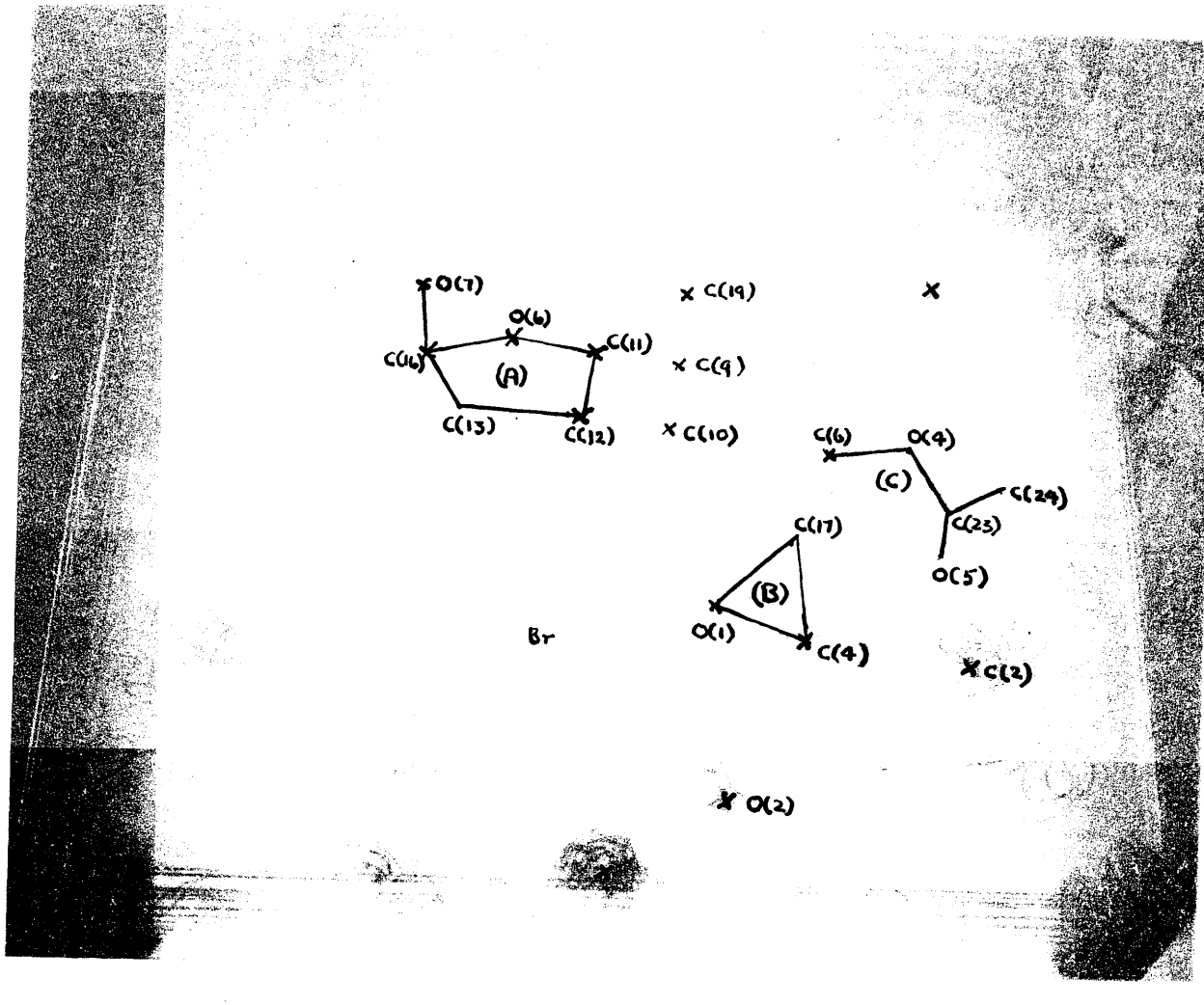
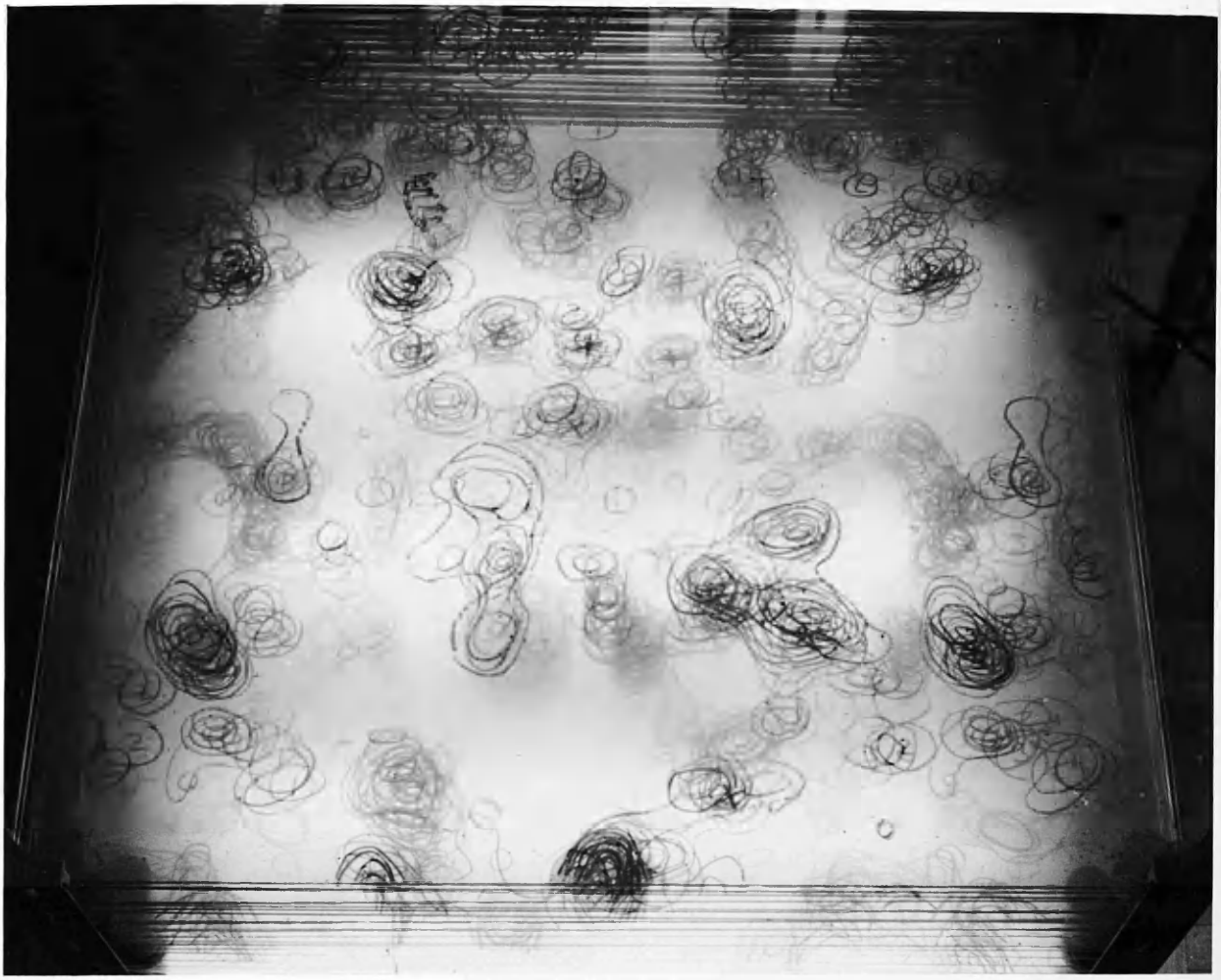


Fig.VI. The First Three-dimensional Fourier Map and Superposition Function. Sections are drawn on glass and the sheets are stacked $\perp^{r}$ to the b-axis. The peaks marked by crosses were those included in the second cycle of calculations. Atoms and chemical fragments referred to in text are shown on tracing sheet. (N.B. These fragments often do not correspond to the equivalent position of the final co-ordinates listed in Table VI.)



$$\rho(XYZ) = {}^{8}/_{V}\Big\{\sum_{0}^{\infty}\sum_{0}^{\infty}\sum_{0}^{\infty}{}^{h+k=2n}\,|F(hk\ell)|\,[\cos 2\pi hX \cos 2\pi kY \cos 2\pi \ell Z \cos\alpha(hk\ell) - \sin 2\pi hX \sin 2\pi kY \sin 2\pi \ell Z \sin\alpha(hk\ell)] - \sum_{0}^{\infty}\sum_{0}^{\infty}\sum_{0}^{\infty}{}^{h+k=2n+1}\,|F(hk\ell)|\,[\sin 2\pi hX \sin 2\pi kY \cos 2\pi \ell Z \cos\alpha(hk\ell) - \cos 2\pi hX \cos 2\pi kY \sin 2\pi \ell Z \sin\alpha(hk\ell)]\Big\}$$

The first Fourier map is shown in Fig.VI with sections perpendicular to the b-axis drawn on glass and built up to give a three-dimensional effect.

There were a great many peaks that could represent possible carbon or oxygen atoms. The most significant structural feature was a five-membered ring (A) (C(11), C(12), C(13), C(16) and O(6)). There was another atom (O(7)) that appeared to be bonded to C(16) of ring (A) but could not be the oxygen of a carbonyl group as one might expect in that position, on account of the angle (O(6)$\hat{C}$(16)O(7)) being tetrahedral. It was difficult to find an atom that could be covalently bonded to the bromine atom; the two nearest peaks seemed to be diffraction 'ripples' due to the presence of the bromine atom and in any case neither seemed to be attached to other atoms. A three-membered ring (B) could also be distinguished and this could well be the epoxide group known to be present in clerodin. Another group of five

atoms (C(6),O(4),C(23),O(5),C(24)) could be discerned in the general shape of an acetate group (C) attached to a carbon atom. On account of lack of experience in this type of work at this time, it was thought better to seek additional evidence for the correctness of atomic positions rather than to include atoms in the phasing calculations that might prove to be false.

III. Three-dimensional Superposition Function.

This three-dimensional function was obtained by placing the origin of the three-dimensional Patterson map, with the coefficients having the form $|F(hk\ell)|^2 M(\underline{S})$, in turn at each bromine position and accepting the minimum value of the four transposed Patterson functions as the value of the superposition function. This function was then drawn up on the same glass sheets as held the three-dimensional electron density distribution. When both functions have a maximum value, there is strong evidence for the presence of a genuine atom. Fifteen such sites were selected as corresponding to atomic positions and these are indicated in Fig.VI.

IV. The Solution of the Structure.

The second structure factor calculation was carried out on fifteen atoms, included with carbon form factors, and the bromine atom. The R-factor was 43%. An electron density distribution calculated on the basis of the phases so obtained is shown in Fig.VII. Some of the smaller peaks apparent in Fourier I had disappeared, and twelve of the fifteen light atoms included in the phasing calculations had come up to satisfactory heights. The five-membered ring seen in Fourier I was clearly genuine as the one atom not included in the phasing calculations was represented by a substantial peak. Similarly, the atom from the three-membered ring not included in the phasing calculations came up to a satisfactory height in the electron density map. The problem of finding the point of attachment of the bromine atom to the rest of the molecule remained unsolved, the distance between the bromine atom and C(13) being 3.02 Å. In addition to the acetate group recognised earlier, the atoms, C(18), O(2), C(21), O(3), C(22), making up a second acetate group (D), could be discerned attached to an atom adjoining C(4) of the epoxide group.

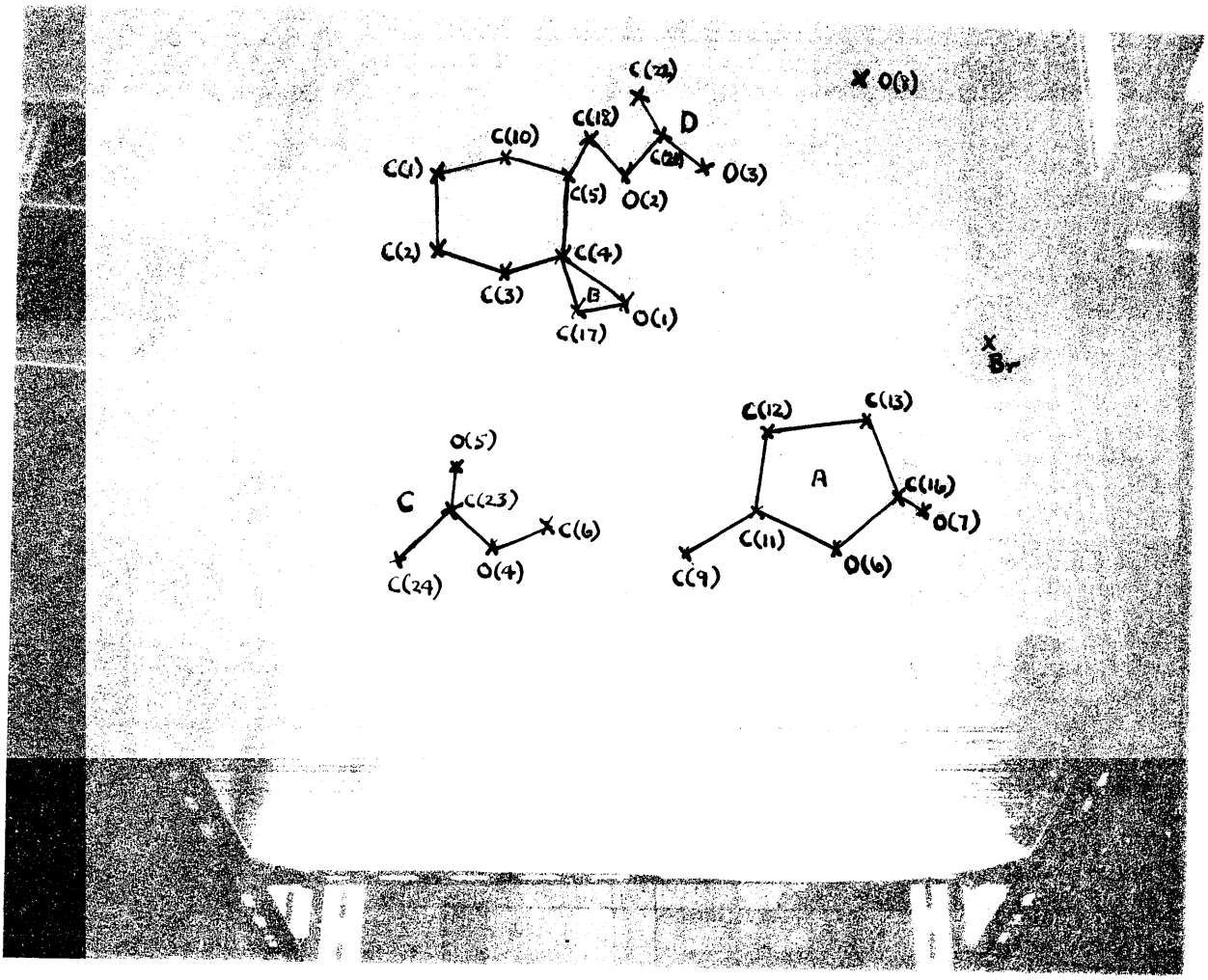
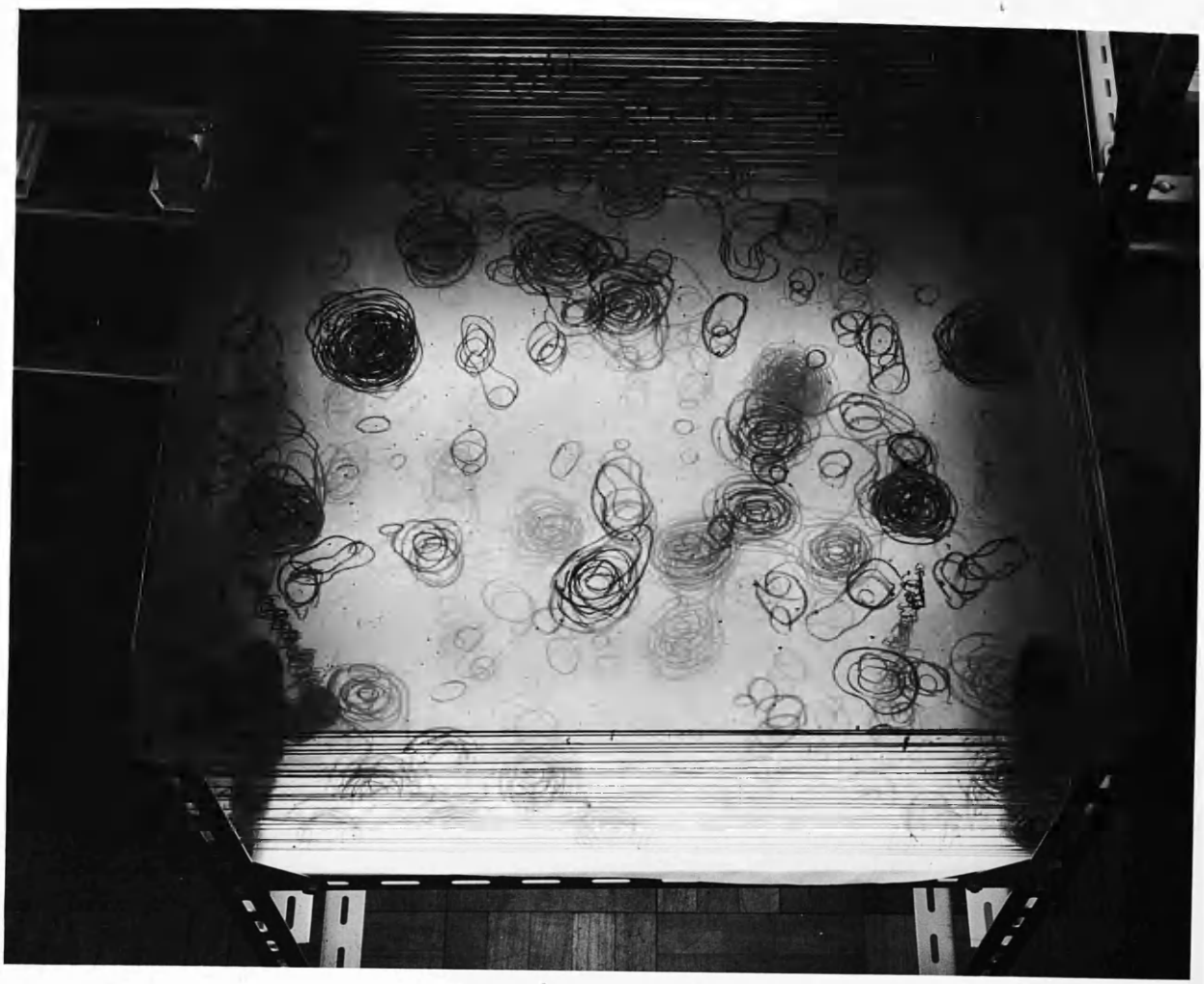
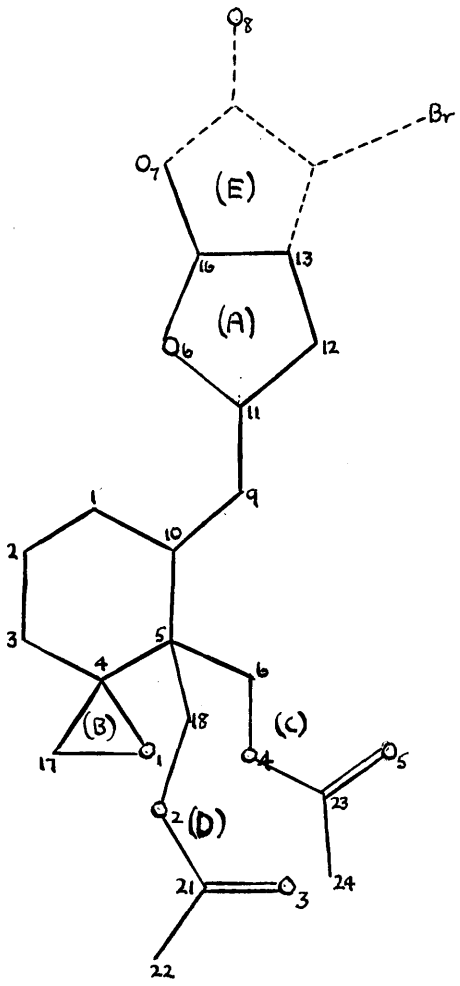


Fig.VII. The Second Three-dimensional Fourier Map. Sections are drawn perpendicular to the b-axis. Atoms and chemical fragments referred to in the text are shown on tracing sheet.





(V)

At this stage the partial structure shown in (V) by the unbroken line could be discerned. This accounted for twenty five of the twenty eight light atoms expected. The main difficulty in accepting this structure was the position of attachment of the bromine atom. If one assumed the presence of a second five-membered ring (E) in the structure (V), to which the bromine atom could be attached, the resulting structure would have the accepted molecular formula, $C_{21}H_{29}O_7Br$. The position of the two acetate groups, however, was most unusual from a chemical point of view, some peaks in the Fourier map were as yet unaccounted for, and the crystallographic evidence for ring (E) was slight (the presence of maxima at C(13), C(16), O(7), and O(8)).

A third structure factor calculation was carried out including fourteen light atoms that were almost certainly

genuine (C(1), C(2), C(4), C(9), C(10), C(11), C(12), C(13), C(16), C(17), O(1), O(6), O(7) and O(8)). Eleven of those atoms had been used in the second structure factor calculation; the three atoms in that calculation that had not come up to reasonable heights were rejected from the third calculation, as was C(6), although it was probably genuine. The R-factor for this third calculation was 42%, and the Fourier map computed on the basis of the phases obtained is shown in Fig. VIII.

All the atoms included in the third structure factor calculation came up to satisfactory heights. Of the three atoms that failed to come up in the second electron density map, two had virtually disappeared and were thus considered to have been spurious detail, but the third peak, C(19), at a possible site near C(9) had a height of 2.8 electrons/Å^3. This peak therefore appeared to represent a genuine atom. All the numbered atoms in the structure (V) had come up to satisfactory heights, whether they were included in the phasing calculations or not, but there were two other peaks, C(7) and C(8), in the electron density map that had a height of 2.15 and 2.18 electrons/Å^3 respectively. There were, therefore, probably three genuine atoms apart from those shown in structure (V). The purely crystallographic evidence for the genuineness

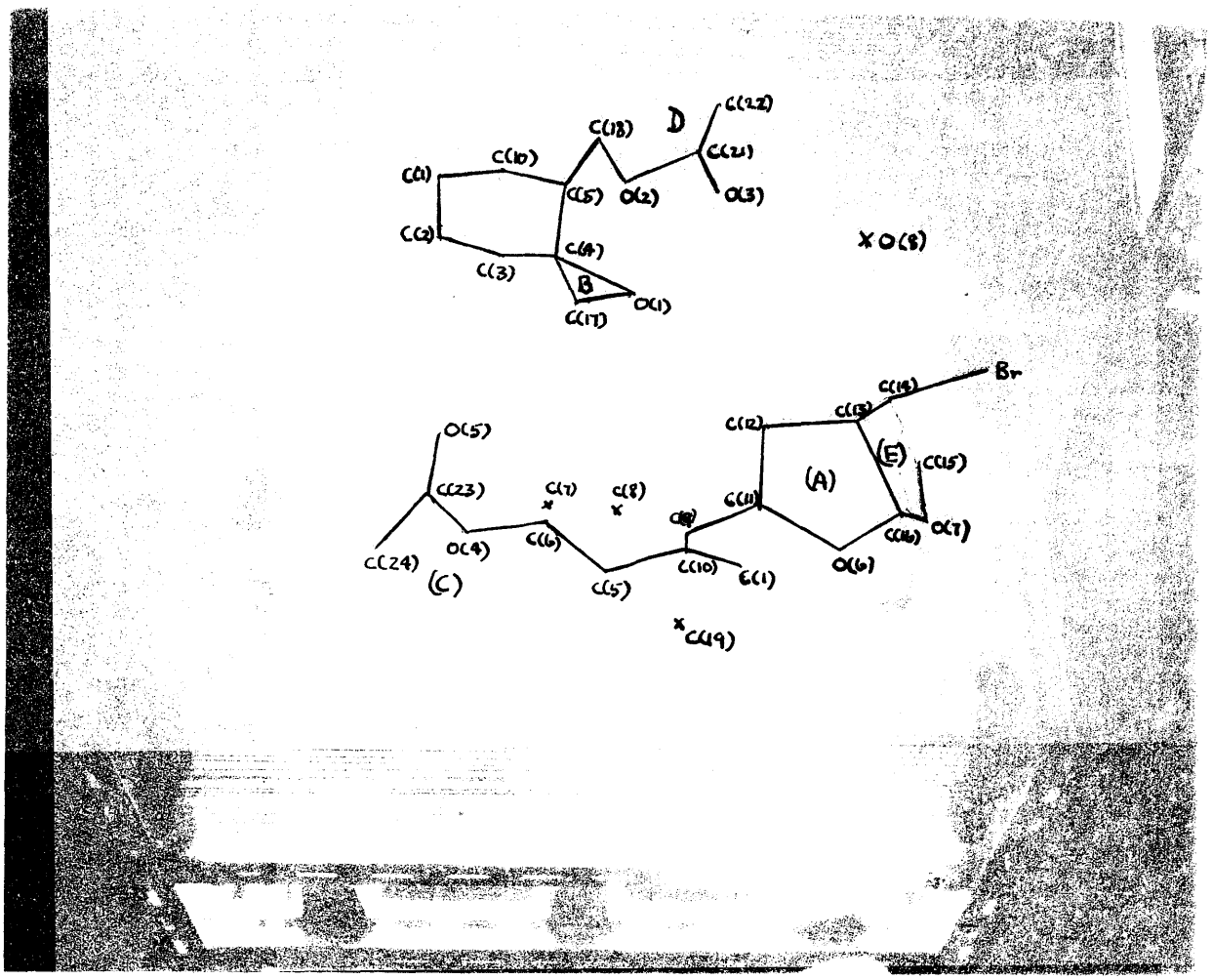
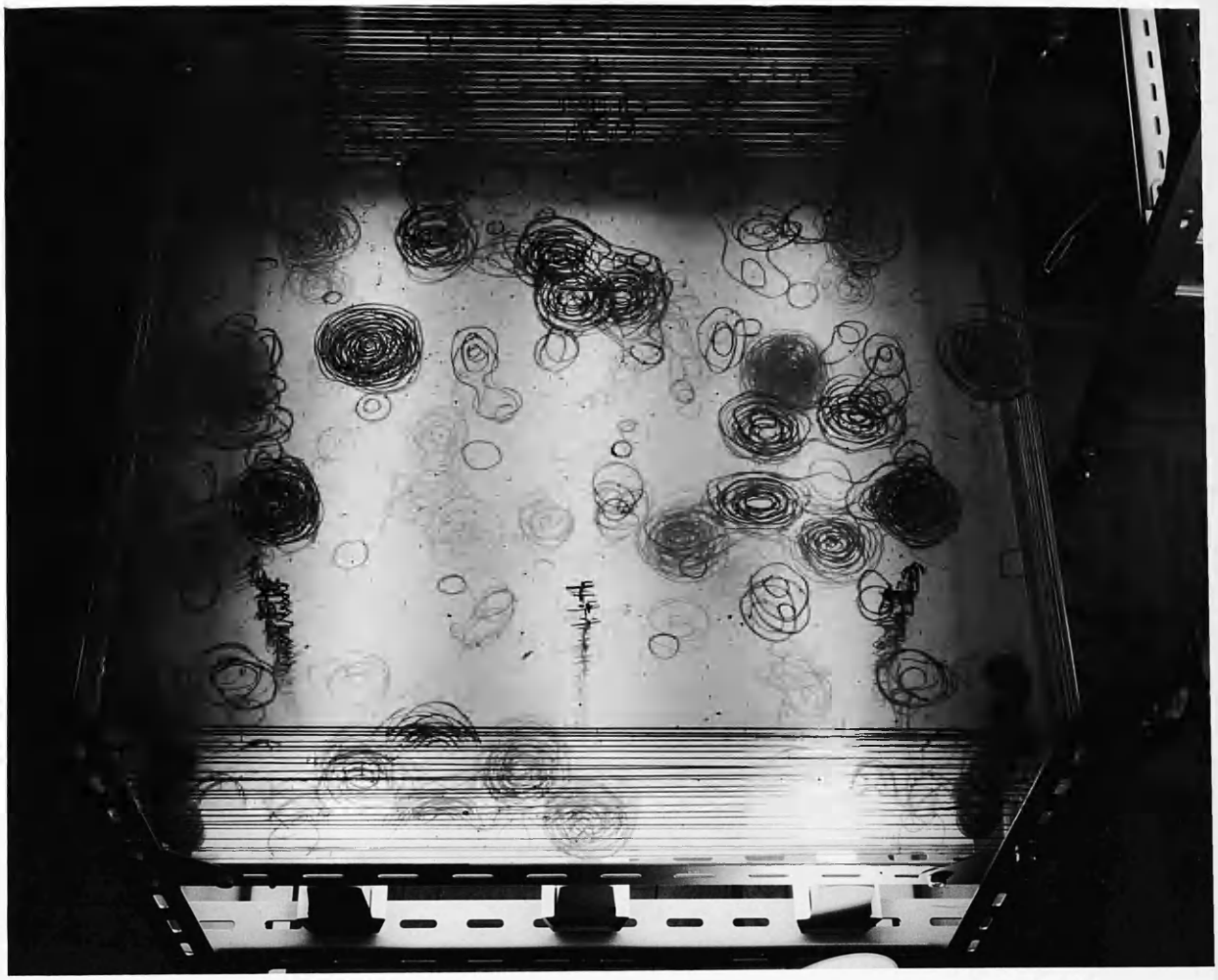


Fig.VIII. The Third Three-dimensional Fourier Map. Sections drawn perpendicular to the b-axis. Atoms and chemical fragments referred to in text are marked on the tracing sheet.



of atoms C(7), C(8), and C(19) was greater than that for the presence of the second five-membered ring (E).

The essential correctness of structure (V) was confirmed by calculating some structure factors for the Okℓ zone of reflexions. All the atoms in structure (V) were included in this calculation, and the discrepancy, between observed and calculated structure factors showed a drop of 8% compared to that for the corresponding reflexions in the third structure factor calculation. Thus, although the two remaining atoms, C(14) and C(15), in ring (E) did not come up to great heights in the electron density map, the sites were probably occupied by genuine atoms. No other attachment of the bromine atom to the structure could be envisaged.

At this stage in the analysis, it was realised that many problems could be solved if the molecular formula of clerodin bromolactone was not $C_{21}H_{27}O_7Br$ as had hitherto been accepted. An accurate density determination on the crystals of clerodin bromolactone was carried out, and it was realised that the molecular weight of clerodin bromolactone should be about 528, which would be consistent with a molecular formula of $C_{24}H_{33}O_8Br$ rather than $C_{21}H_{27}O_7Br$. The corresponding formula for clerodin would be $C_{24}H_{34}O_7$ rather than $C_{21}H_{28}O_6$, and it can be appreciated that these two

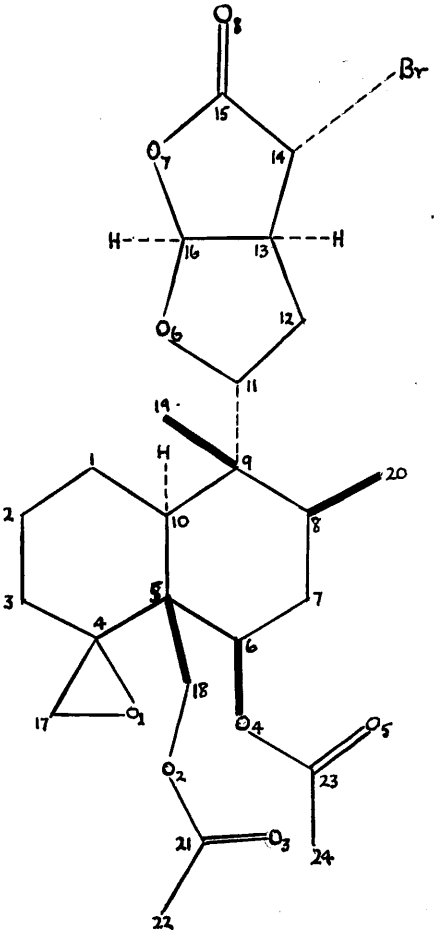
alternative formulae would give similar analytical data. Examination of various clerodin derivatives, supplied by Professor Barton, was carried out by Dr. R.I.Reed of this department, using the mass spectrograph. The results obtained were consistent with the $C_{24}H_{34}O_7$ formula for clerodin.

Meanwhile, a fourth set of structure factors had been calculated and an electron density map had been computed. Twenty one light atoms (C(1), C(2), C(3), C(4), C(5), C(6), C(9), C(10), C(11), C(12), C(13), C(16), C(17), C(18), C(21), C(22), O(1), O(2), O(3), O(5), and O(6)) were included in the calculation and the resulting R-factor was 40%. More stringent requirements were demanded before including a term in the Fourier synthesis than had been the case previously. This resulted in ninety eight reflexions being omitted from the Fourier map, which gave a much clearer representation of the structure.

The atoms of the second five-membered ring (E) had been omitted from the calculations, yet the heights at the sites of C(14), C(15), O(7) and O(8) were 2.89, 2.63, 4.60 and 3.95 electrons/$\mathring{A}^3$ respectively. This would appear to be conclusive proof of the existence of the second five-membered ring. All the other atoms in

structure (V) came up to heights greater than 2.5 electrons/$\mathring{A}^3$, while the three atoms, C(7), C(8) and C(19), not in that structure but which had shown up in the third Fourier map were clearly genuine. Thirty one of the thirty two light atoms had therefore been identified. The remaining atom was most probably attached to C(8) in a position CIS to C(19), although there was some evidence for the opposite configuration at C(8).

A fifth cycle of structure factor and Fourier calculations including thirty one light atoms and the bromine atom in the phasing calculations clearly revealed C(20) to be in the equatorial position attached to C(8) and hence CIS to C(19) on C(9). The distinction between carbon and oxygen atoms could be clearly drawn in all cases except that of the epoxide group where the configuration remained in doubt. Apart from this point, the structure and relative stereochemistry of clerodin bromolactone are shown in (VI).


O8
Br
15
O7
14
H
16
13
H
O6
12
11
19
H
9
1
20
2
10
8
3
5
7
4
6
18
17
O1
O4
O5
O2
23
21
O3
24
22

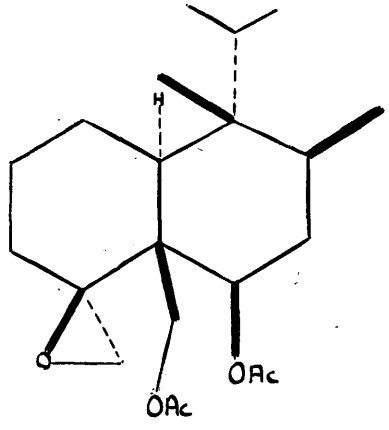
(VI)

V. Refinement by Fourier Methods.

The discrepancy at the fifth structure factor calculation was 32%. The positions of the atoms in the epoxide group obtained from the fifth Fourier synthesis gave bond lengths which suggested one configuration while the peak heights in this map tended to indicate the opposite configuration. After two further cycles of structure factor and Fourier calculations, the R-factor was 29%, but the ambiguity concerning the configuration of the epoxide group remained. At the seventh cycle of calculations, a Fourier synthesis was also computed with the calculated structure factors as coefficients and the new co-ordinates were found by Booth's 'back-shift' method. The temperature factors of all the atoms were increased so that B_θ equaled 4. The next structure factor calculation gave a reduction of the discrepancy to 24%.

Three further cycles of refinement employing F_o and F_c Fourier syntheses and Booth's 'back-shift' correction reduced the R-factor to 21.5%. The stereochemistry of the epoxide group still remained in doubt. One of the atoms comes up to a height of 5.35 electrons/$\mathring{A}^3$ in the F_o synthesis and to a height of 5.34 electrons/$\mathring{A}^3$ in the F_c synthesis. As both atoms were included in the

calculations as carbon atoms, it would seem that this atom is a carbon atom. The other atom has a height of 6.52 electrons/$\mathring{A}^3$ in the F_o synthesis and a height of 5.87 electrons/$\mathring{A}^3$ in the F_c synthesis, from which evidence it would seem that this atom is an oxygen atom. Contrary to this, however, the bond between C(4) and the first atom is 1.48 $\mathring{A}$, and that between C(4) and the second atom is 1.52 $\mathring{A}$, whereas the distance of a C - O single bond should be slightly shorter than that of a C - C single bond. This anomaly between the peak heights and bond lengths in the epoxide group has persisted throughout the last five cycles of structure factor and Fourier calculations. Chemical evidence (Barton, 1961) suggests that the configuration of the epoxide is that shown in (VII). This stereochemistry would suggest that the evidence of the peak heights in assigning the nature of the atoms is more reliable than that of the bond lengths.



(VII)

VI. Refinement By Least Squares.

The progress of the refinement shown in Table II suggests that the maximum effectiveness of the Fourier method has been reached. There is evidence from the Fourier maps that the bromine atom has a pronounced anisotropic thermal vibration in the y- direction. Such thermal motion can best be taken into account by the Deuce Least Squares program.

The data was not considered sufficiently good to permit the location of hydrogen atoms and the contribution of these atoms was not considered at any time in the refinement. Three cycles of least squares refinement were undertaken on all the observed data, employing the following weighting scheme:

$$\sqrt{w(hk\ell)} = \frac{|F_o(hk\ell)|}{54.00} \quad \text{if } |F_o| < 54.00$$

$$\text{and } \sqrt{w(hk\ell)} = \frac{54.00}{|F_o(hk\ell)|} \quad \text{if } |F_o| > 54.00.$$

This reduced $\Sigma w\Delta^2$, the quantity being minimised, from 1572 to 872 and gave for the light atoms an average standard deviation in atomic position of 0.034 Å. The R-factor calculated on the output of the third cycle of least squares was 17.2%. The lengths of the bonds in the epoxide ring remained anomalous. A further cycle of least squares refinement was carried out on the

positional and thermal parameters, produced by the third cycle, using a different weighting scheme, where, if

$$|F_o| < 54.0 \ , \ \sqrt{w(hk\ell)} = 1$$

and if $|F_o| \geq 54.0 \ , \ \sqrt{w(hk\ell)} = \dfrac{54.0}{|F_c(hk\ell)|}$

The value of $\sum w\Delta^2$ produced by this cycle was 1240 and the average estimated standard deviation in the positional parameters was 0.029 Å. The R-factor obtained by calculating structure factors on the output of this calculation was 16.0%. In the course of the four cycles of least squares refinement all the atoms were included with anisotropic temperature factors, that for bromine being very pronounced in the y- direction.

The bond lengths and anisotropic temperature parameters for the epoxide group obtained from the output from the fourth least squares cycle are shown in Table III.

Throughout the least squares refinement, the atom with the higher peak height in the last F_o synthesis, O(1), has been included as an oxygen atom. The bond lengths in the epoxide group remained anomalous, although the temperature parameters did not suggest an incorrect assignment.

Additional evidence for the configuration of the epoxide group shown in (VII) was provided by sections

TABLE III.

Bond Lengths.

C(4) - C(17)	1.473 Å
C(4) - O(1)	1.499 Å
C(17) - O(1)	1.473 Å

Anisotropic Temperature Parameters.

	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23} ($\times 10^5$)
C(17)	938	1901	285	386	484	525
O(1)	1270	2032	264	673	-44	206

of three-dimensional difference syntheses (Fig.IX) and by temperature factors resulting from further least squares refinement in which C(17) and O(1) were weighted

(i) as carbon and oxygen atoms respectively,

(ii) as oxygen and carbon atoms respectively, and

(iii) with both atoms as carbon atoms.

TABLE IV.

Anisotropic Thermal Parameters (bij x 10^5) for atom C(17) and O(1) of the epoxide ring. These parameters derive from the least squares procedures.

(i) C(17) weighted as carbon and O(1) as oxygen.

(ii) C(17) weighted as oxygen and O(1) as carbon.

(iii) C(17) weighted as carbon and O(1) as carbon.

		b_{11}	b_{22}	b_{33}	b_{12}	b_{23}	b_{13}
	(i)	1323	2466	330	385	1236	472
C(17)	(ii)	3630	3364	654	1249	1229	1146
	(iii)	2800	2081	405	1672	1425	1307
	(i)	697	3910	259	1356	214	-401
O(1)	(ii)	-928	2401	55	588	-36	-390
	(iii)	-758	2358	18	1128	169	-246

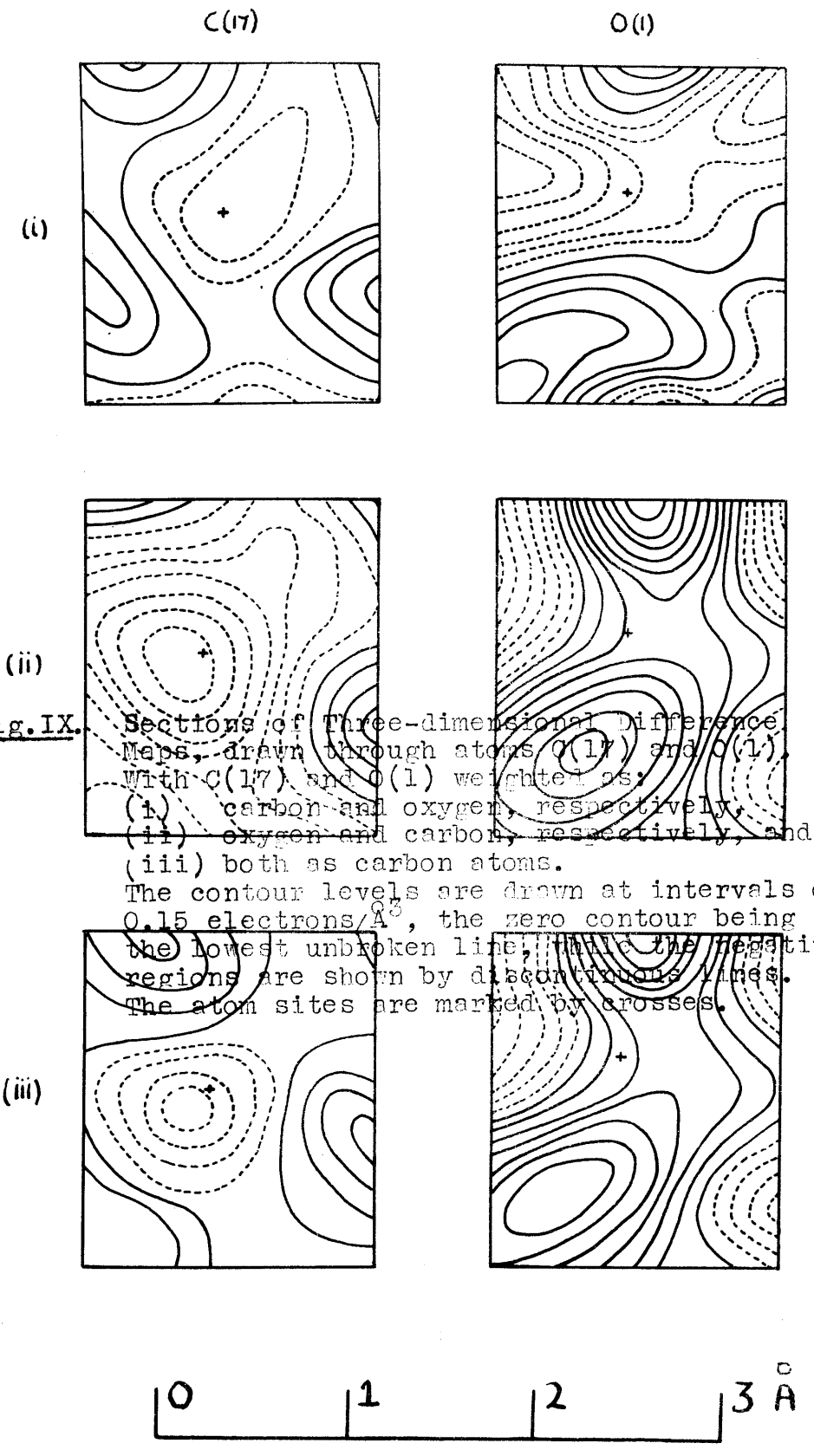
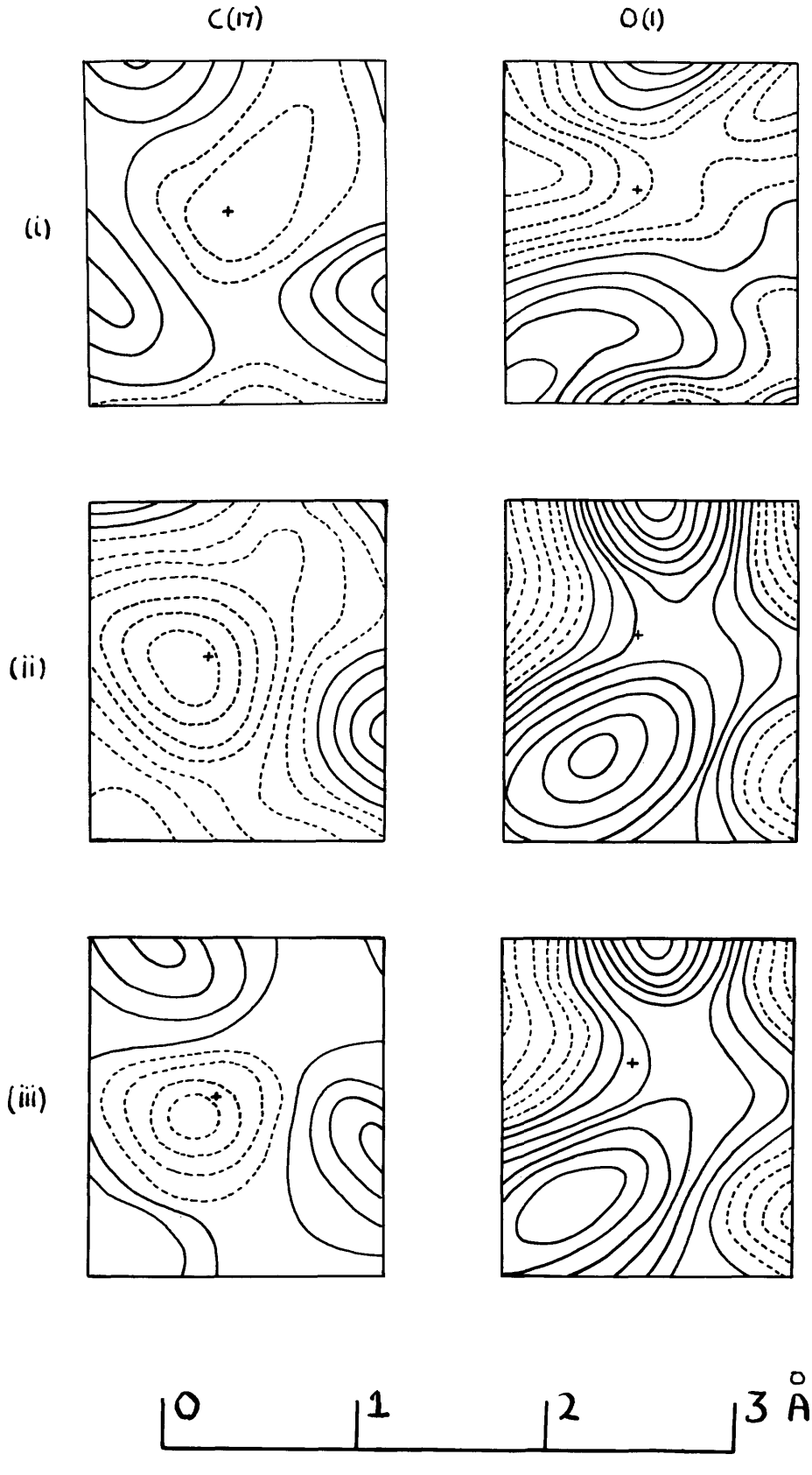


Fig.IX. Sections of Three-dimensional Difference Maps, drawn through atoms C(17) and O(1), with C(17) and O(1) weighted as:
(i) carbon and oxygen, respectively,
(ii) oxygen and carbon, respectively, and
(iii) both as carbon atoms.
The contour levels are drawn at intervals of 0.15 electrons/$Å^3$, the zero contour being the lowest unbroken line, while the negative regions are shown by discontinuous lines. The atom sites are marked by crosses.


C(17)
O(1)
(i)
(ii)
(iii)
0
1
2
3 Å

Three cycles of least squares were performed with each of the above assignments; the positional and anisotropic thermal vibrations of the other atoms were not refined. With C(17) weighted as a carbon atom and O(1) as an oxygen atom, the R- factor was reduced to 15.7%, the final value of $\Sigma w\Delta^2$ being 688. The temperature factors produced for the two atoms were acceptable. Sections of a difference synthesis (Fig. IX(i)) calculated on the structure factors obtained with the latest set of co-ordinates showed that both atoms lay in negative regions of the map, C(17) at a value of -0.32 electrons/$\mathring{A}^3$ and O(1) at a value of -0.54 electrons/$\mathring{A}^3$.

With C(17) weighted as oxygen and O(1) as carbon, a similar procedure was followed. The R-factor was not reduced below 17.1% and the final value of $\Sigma w\Delta^2$ was 832. The temperature factors showed extremely high values for C(17) and low values (even negative ones) for O(1), suggesting that the assignment of chemical type is incorrect. Difference maps (Fig. IX(ii)) through the two atoms showed that C(17) was lying in a negative region of the map ($\rho_o - \rho_c$ = -1.12 electrons/$\mathring{A}^3$) whereas O(1) lay in a positive region ($\rho_o - \rho_c$ = +0.32 electrons/$\mathring{A}^3$).

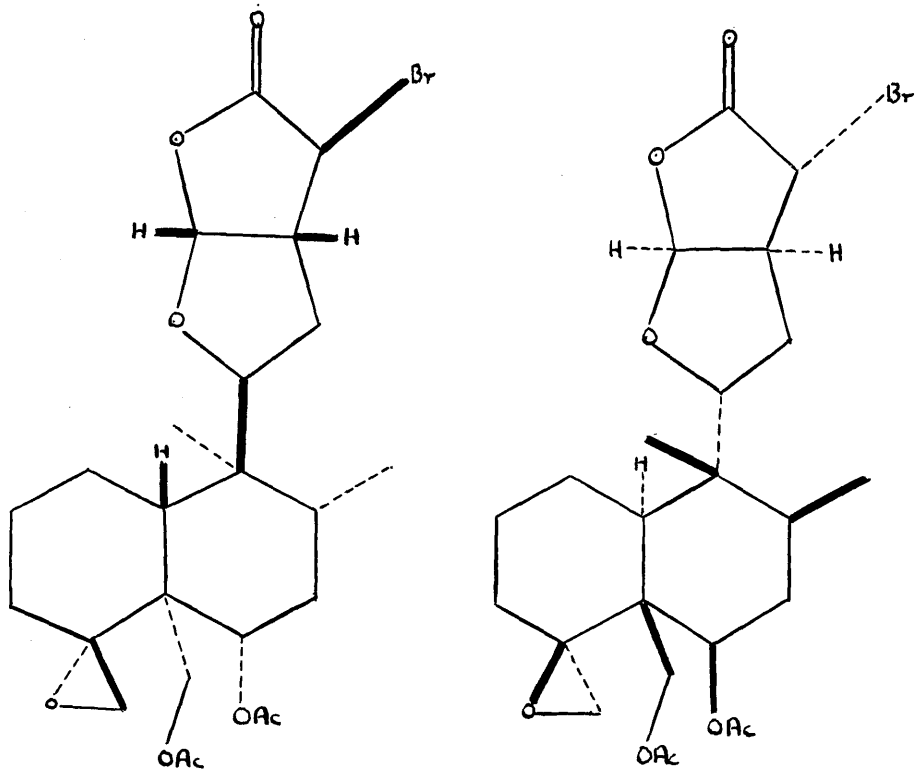
Finally, when both atoms were included as carbon atoms, the R-factor was not reduced below 16.6% and the final value of $\Sigma w\Delta^2$ was 736. The temperature

factor output showed smaller values for C(17) than in (ii) but the values for O(1) were still very small and b_{11} was negative. The difference maps (Fig.IX(iii)) through the two atoms showed that C(17) lay in a negative region ($\rho_o - \rho_c = -0.54$ electrons/Å^3) while O(1) was in a similar position to the one it had been in (ii).

These results all tend to indicate that O(1) is indeed the oxygen atom, and C(17) is the carbon atom of the epoxide group and that the configuration of the epoxide group is that shown in (VII).

VII. Absolute Configuration.

The intensities of the (1kℓ) zone of reflexions were examined for evidence of anomalous dispersion, differences being observed in the cases of six reflexions which should have had equal intensity in the absence of anomalous scattering. (Table V). By careful attention to the geometric aspects of recording the intensities and on the basis of a right-handed co-ordinate system, the indexing is as shown in Fig.(X). With the co-ordinate system defined, the enantiomorph present can be found by calculating the $|F(hk\ell)|^2$ and $|F(\bar{h}\bar{k}\bar{\ell})|^2$ values on the basis of anomalous scattering by the bromine atom. If the calculated values of $|F|^2$ so obtained support the observed differences in intensity, the enantiomorph used for the calculation is the form actually present in the crystal. On the other hand, if the calculated values of $|F|^2$ are in the opposite sense to the observed intensities, the mirror image of the form used in the calculations is the true enantiomorph. The calculations carried out until now have all been on the enantiomorph shown in (VIII (a)). The results obtained in Table V, with one exception, contradict the observed values suggesting that the absolute configuration is that shown in (VIII(b)). The one exception is the 1, 2, 18 reflexion. The



(a) (b)

(VIII)

difference between the calculated values of $|F(hk\ell)|^2$ and $|F(\bar{h}\bar{k}\bar{\ell})|^2$ is small and the error is almost certainly due to the poor agreement between $|F_o|$ and $|F_c|$ for this reflexion (Table XIII). This high discrepancy (50%) could well result in errors in A_o and B_o due to the uncertainty in the phase. Incorrect A_o and B_o values could result in errors in the $|F(hk\ell)|$ and $|F(\bar{h}\bar{k}\bar{\ell})|$ for this reflexion. The full calculation is shown in Table V.

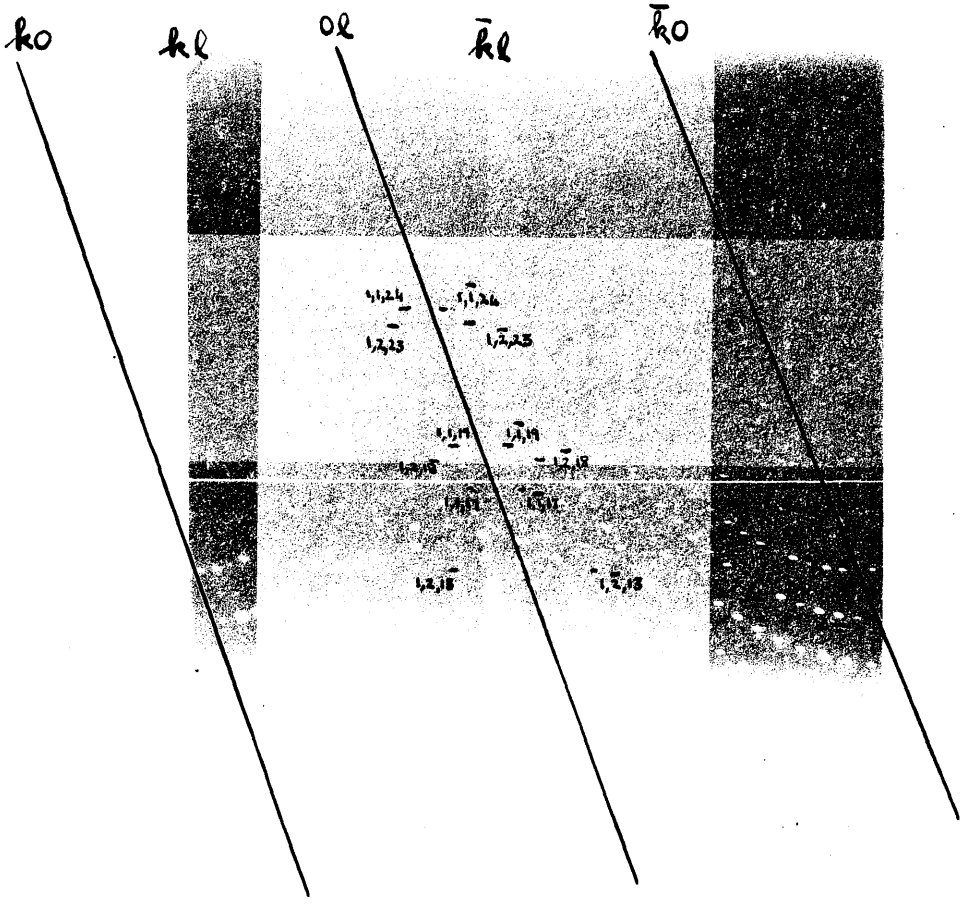


FIG. X.

Negative Print of X-ray Moving Film Photograph of 1KL zone. The indexing is as shown on tracing sheet, and the reflexions marked are those on which the determination of absolute configuration was based.

FIG. X.

Negative Print of X-ray Moving Film Photograph of 1KL zone. The indexing is as shown on tracing sheet, and the reflexions marked are those on which the determination of absolute configuration was based.

TABLE V.

Calculation of the values of $|F(hk\ell)|^2$ and $|F(\bar{h}\bar{k}\bar{\ell})|^2$ [$\Delta f' = -0.9$; $\Delta f'' = 1.5$. Dauben and Templeton,(1955)].

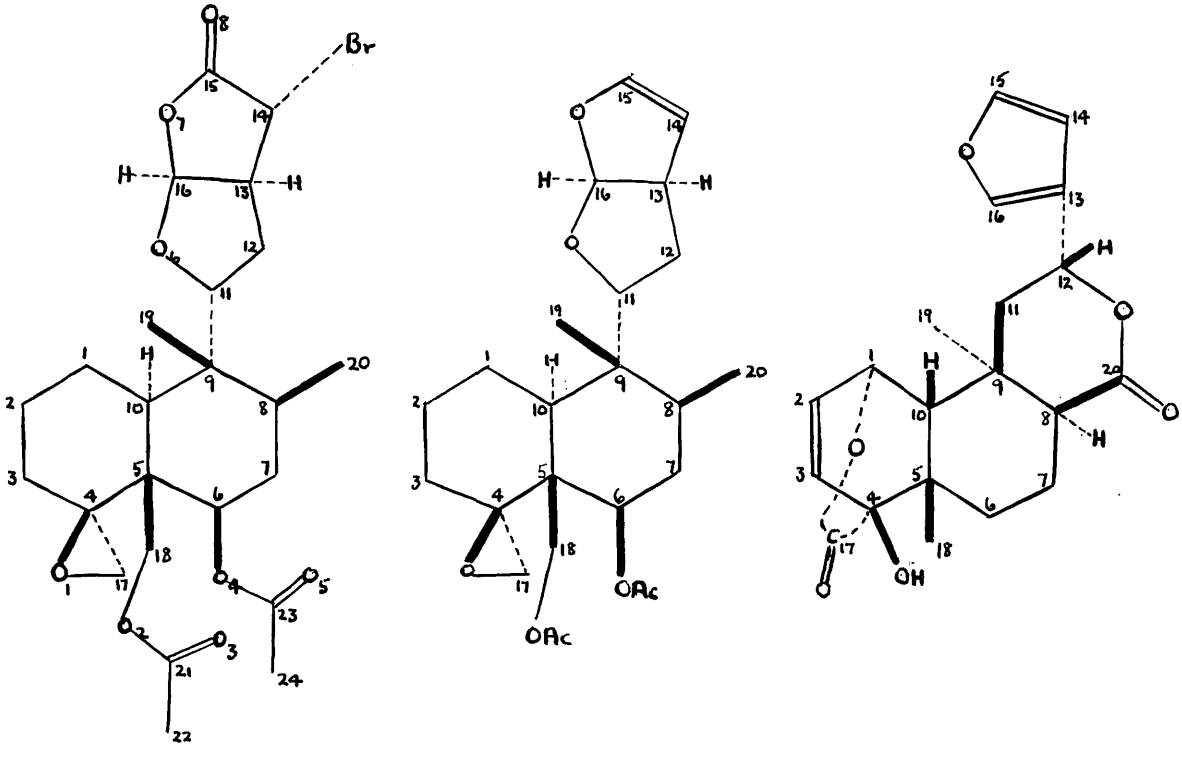
Reflexion	Geometric Part of Br. Contribution	Real Part of Correction	Imaginary Part of Correction.
1 1 17	$-2.09 \pm i\ 0.63$	$+0.18 \mp i\ 0.05$	$\mp 0.09 - i\ 0.29$
1 1 19	$+1.52 \mp i\ 2.22$	$-0.15 \pm i\ 0.22$	$\pm 0.37 + i\ 0.25$
1 1 24	$\mp 1.49 + i\ 2.18$	$\pm 0.26 - i\ 0.38$	$-0.62 \mp i\ 0.42$
1 2 13	$\pm 1.58 - i\ 1.01$	$\mp 0.09 + i\ 0.06$	$+0.10 \pm i\ 0.16$
1 2 18	$+1.41 \mp i\ 1.00$	$-0.13 \pm i\ 0.09$	$\pm 0.16 + i\ 0.22$
1 2 23	$\pm 0.98 - i\ 1.16$	$\mp 0.16 + i\ 0.19$	$+0.32 \pm i\ 0.27$

$A_o + B_o$	$A_o + B_o$ + Real corrn.	$A_o + iB_o(hk\ell)$	$A_o + iB_o(\bar{h}\bar{k}\bar{\ell})$
$+2.28 \mp i6.88$	$+2.46 \mp i6.93$	$+2.37 - i7.22$	$+2.55 + i6.64$
$+2.76 \pm i9.48$	$+2.61 \pm i9.70$	$+2.98 + i9.95$	$+2.24 - i9.45$
$\pm 2.16 + i6.84$	$\pm 2.42 + i6.46$	$+1.80 + i6.04$	$-3.04 + i6.88$
$\pm 11.20 - i1.00$	$\pm 11.11 - i0.94$	$+11.21 - i0.78$	$-11.01 - i1.10$
$+7.08 \mp i10.08$	$+6.95 \mp i9.99$	$+7.11 - i9.77$	$+6.97 + i10.21$
$\mp 0.16 - i7.32$	$\mp 0.32 - i7.13$	$0 - i6.91$	$+0.64 - i7.40$

$F^2(hk\ell)$	$F^2(\bar{h}\bar{k}\bar{\ell})$	Intensity (obs.)
57.8	50.6	$I(1,1,17) < I(\bar{1},\bar{1},\bar{17})$
107.9	94.3	$I(1,1,19) < I(\bar{1},\bar{1},\bar{19})$
39.7	56.6	$I(1,1,24) > I(\bar{1},\bar{1},\bar{24})$
126.3	122.4	$I(1,2,13) < I(\bar{1},\bar{2},\bar{13})$
146.0	150.3	$I(1,2,18) < I(\bar{1},\bar{2},\bar{18})$
47.7	55.1	$I(1,2,23) > I(\bar{1},\bar{2},\bar{23})$

Results and Conclusions.

The structures of clerodin bromolactone and clerodin are shown in (IX (a) and (b)). Both cyclohexane rings of the trans-decalin system have the chair conformation.



(a) (b) (c)

(IX)

The 19-methyl group is axial and the 20-methyl group is equatorial. The 6-acetoxy substituent is equatorial.

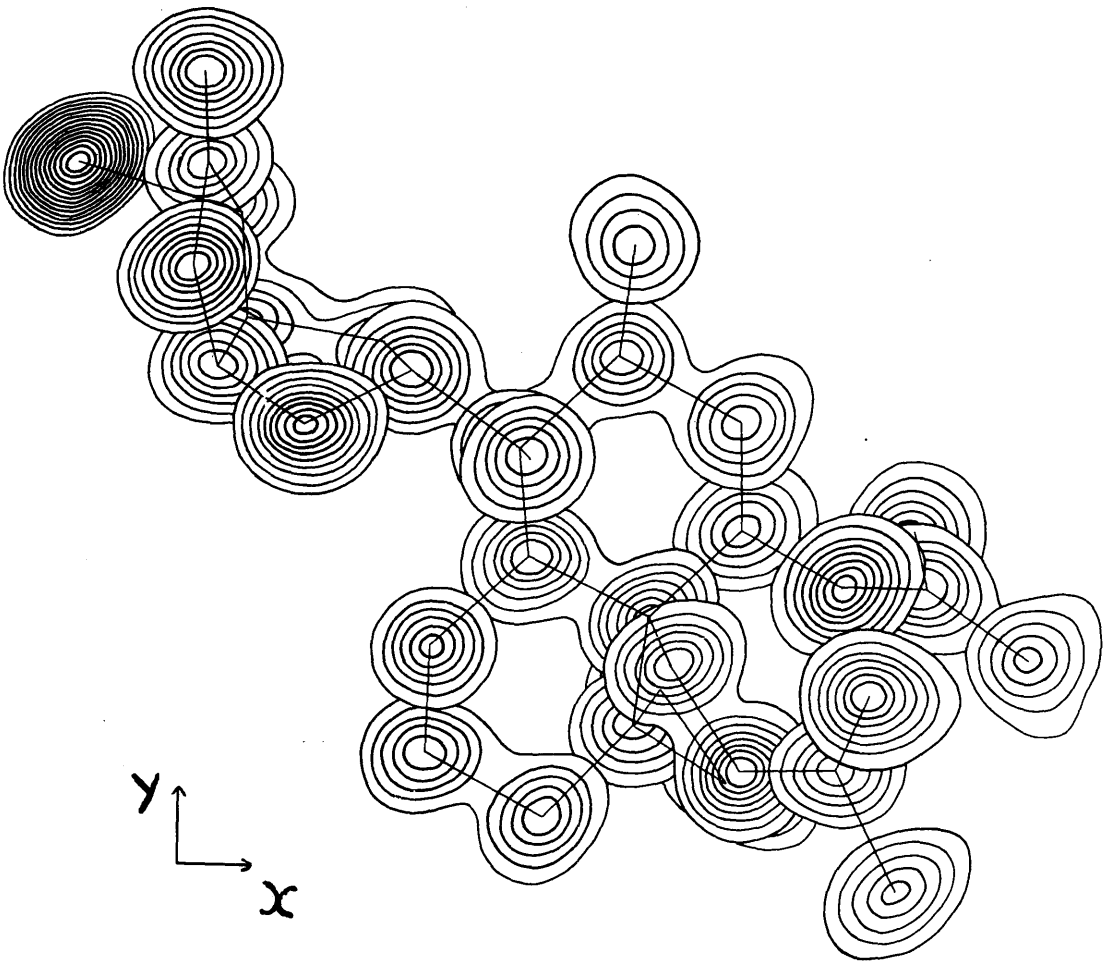


Fig.XI. Superimposed Contour Sections of the final three-dimensional Fourier map, covering the region of one molecule. The sections are drawn parallel to (001). Contours are drawn at 1 electron/Å^3 intervals, with the 1 electron/Å^3 contour omitted. For the bromine atom, the levels are at 3 electron/Å^3 intervals.

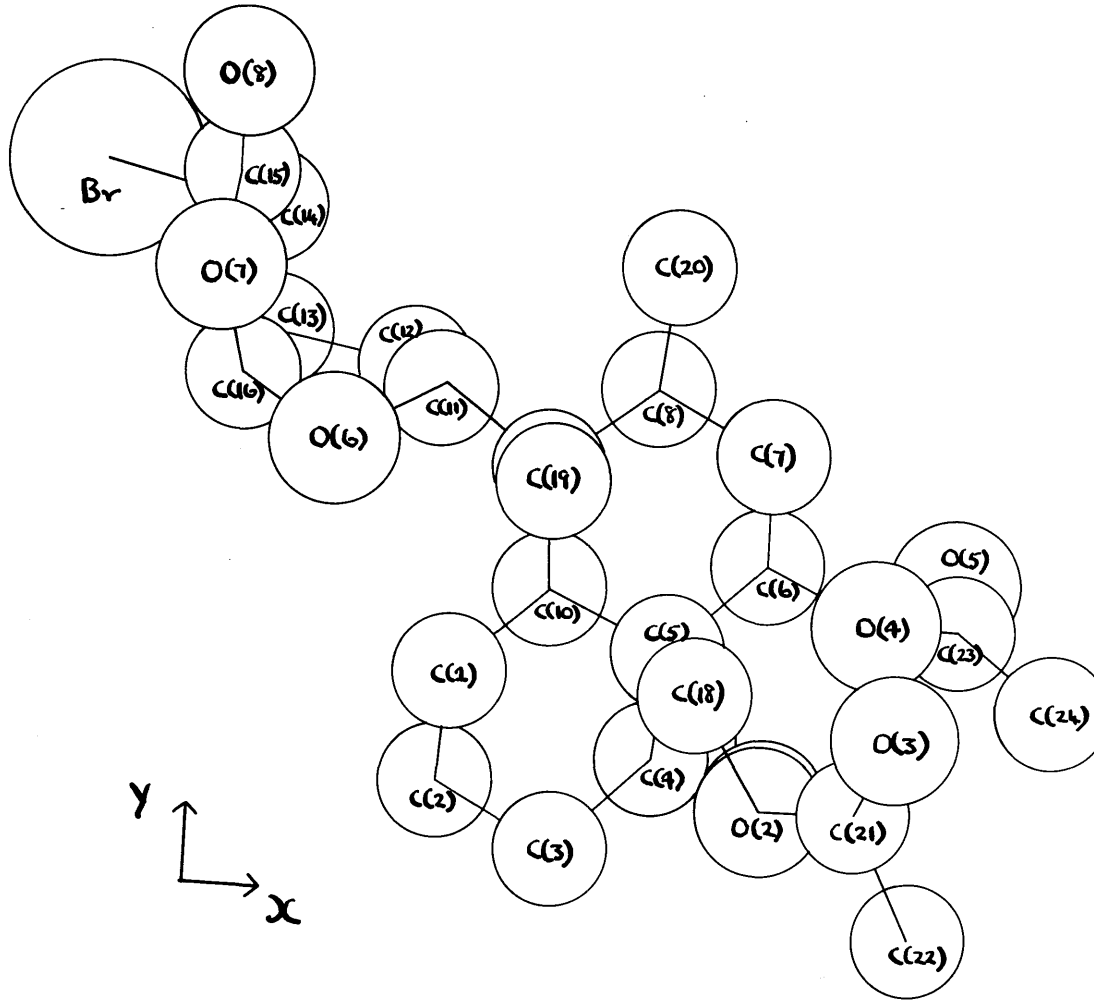
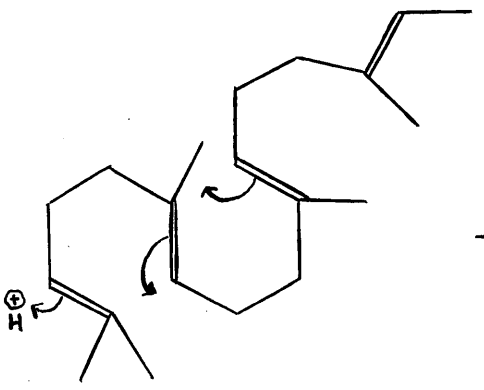


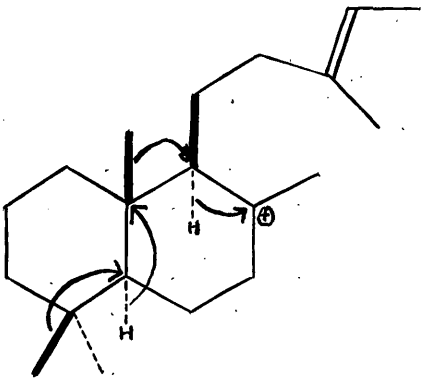
Fig.XII. Explanatory Diagram for Fig.XI, illustrating the atomic arrangement. The atoms are marked on the figure, except in the case of C(9), C(17), and O(1), which are hidden.

The final three-dimensional electron density map is shown in Fig. XI as superimposed contour sections drawn parallel to (0,0,1) and covering the region of one molecule. (This drawing corresponds to the correct absolute configuration.) The corresponding atomic arrangement is illustrated in Fig.XII.

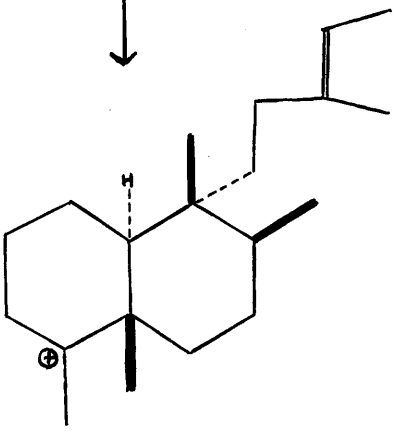
The absolute configuration of clerodin conforms to that expected from the theory of biogenesis as applied to diterpenes. The basic skeleton can be obtained by closure of the chain containing four isoprene units, linked in the normal 'head to tail' manner (X). The relative stereochemistry at C(5), C(8), C(9) and C(10) can then be explained by the occurrence of a series of 1:2-diaxial shifts (XI) and (XII). The formation of the two fused hydrofuran rings may take place by way of allylic oxidation of C(11), C(15) and C(16) to form (XIV). The attack of the (-OR) grouping at C(6) would then be expected to occur from the least hindered side. That this does occur may be appreciated from Fig.XIV, where attack from an axial position would involve interaction with the epoxide and furan ring systems. The stereochemistry of another diterpene, columbin (IX(c)) (Overton, Weir and Wylie, 1961) would suggest that the biogenesis of columbin must differ from that of clerodin.



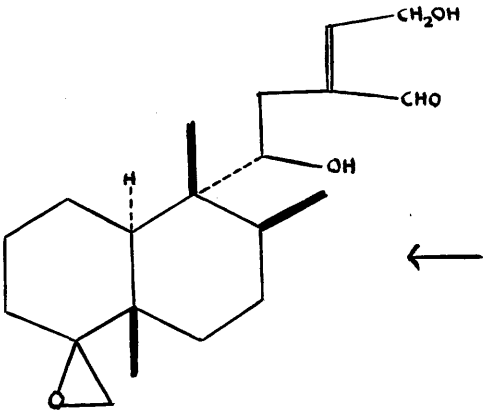
(X)



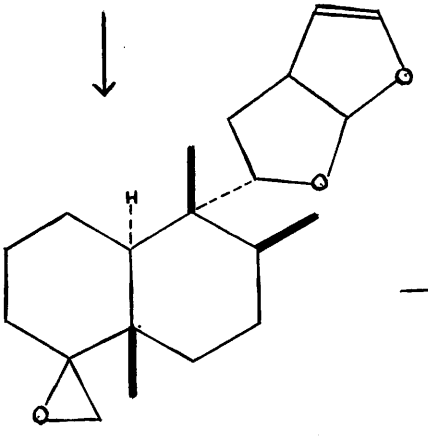
(XI)



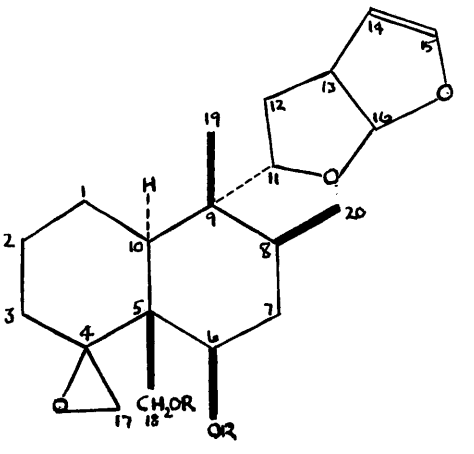
(XII)



(XIII)



(XIV)



(XV)

The final atomic co-ordinates obtained from the fourth least squares cycle are shown in Table VI, while the standard deviations in atomic positions calculated from the least squares output are listed in Table VII. These atomic co-ordinates refer to the opposite enantiomorph to that now known to represent the absolute configuration of clerodin bromolactone. The interatomic bond lengths are listed in Table VIII, while the interbond angles are given in Table IX. The standard deviation, $\sigma(A\text{-}B)$, of a bond between atoms (A) and (B) is given by the formula,

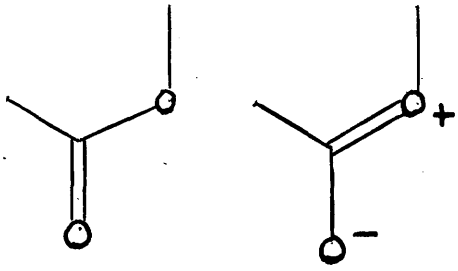
$$\sigma(A\text{-}B)^2 = (\sigma_A^2 + \sigma_B^2)$$

where $\sigma(A)$ and $\sigma(B)$ are the standard deviations in co-ordinates of the atoms (A) and (B). The standard deviation, $\sigma(\beta)$ in radians, for an angle (β) formed at atom (B) by the atoms (A) and (C) is given by the formula,

$$\sigma^2(\beta) = \frac{\sigma^2(A)}{(AB)^2} + \sigma^2(B)\left(\frac{1}{(AB)^2} - \frac{2\cos\beta}{AB.BC} + \frac{1}{(BC)^2}\right) + \frac{\sigma^2(C)}{(BC)^2}$$

The average standard deviation for a C-C single bond is 0.04 Å, while that for a typical tetrahedral angle

is 2.1°. The average C-C single bond is 1.56 Å, not differing significantly from the value of 1.545 Å in diamond. The C-O single bonds, adjacent to a C=O double bond as in (XVI (a)), have a mean length of 1.344 Å whereas the other C-O single bonds have a mean length of 1.469 Å. This difference would seem to indicate that in lactone and ester groups, as in carboxylic acids, the resonance structure shown in (XVI(b)) makes an important contribution. The average C-O bond length in the epoxide group is 1.49 Å differing only slightly from the values found in ethylene oxide (Cunningham, Boyd, Myers, Gwinn, and Le Van, 1951) and cyclopentene oxide (Erlandsson, 1955) of 1.44 Å and 1.47 Å respectively. The C-Br distance of 2.06 Å is somewhat greater than the value of 1.94 Å obtained in the alkyl bromides (Sutton et al., 1958). This difference may well be due to inaccuracies in the positioning of C(14) owing to the close proximity of the bromine atom and the presence of the associated diffraction effects.



(a) (b)

(XVI)

The average bond angle in the decalin system is $109^{o}44'$ comparing well with the value for a tetrahedral angle of $109^{o}28'$. In the five-membered ring comprising C(11), C(12), C(13), C(16), and O(6), the average bond angle is 105^{o}, significantly lower than expected.

Some important intramolecular contacts are shown in Table X. The distances across the cyclohexane rings are on the average 3.00 Å. The distance between C(18) and C(19) is 3.01 Å, longer than would be expected from a model and indicates considerable forces pushing these atoms apart.

The packing of molecules over two full unit cells viewed in projection down the a- and b- axes is shown in Figs. XIII and XIV respectively by means of line drawings of the molecular framework. Any intermolecular contacts less than 4 Å are listed in Table XI, the shortest contact being between C(18) and O(7) at a distance of 3.11 Å, while the shortest intermolecular contact between two carbon atoms is that of 3.58 Å between C(15) . . . . C(22).

The final anisotropic temperature factors are listed in Table XII. These parameters are the values of b_{ij} in the equation:

$$\exp(-B_{\theta} \sin^2\theta/\lambda^2) = 2^{-(b_{11}h^2 + b_{22}k^2 + b_{33}\ell^2 + b_{12}hk + b_{13}h\ell + b_{23}k\ell)}$$

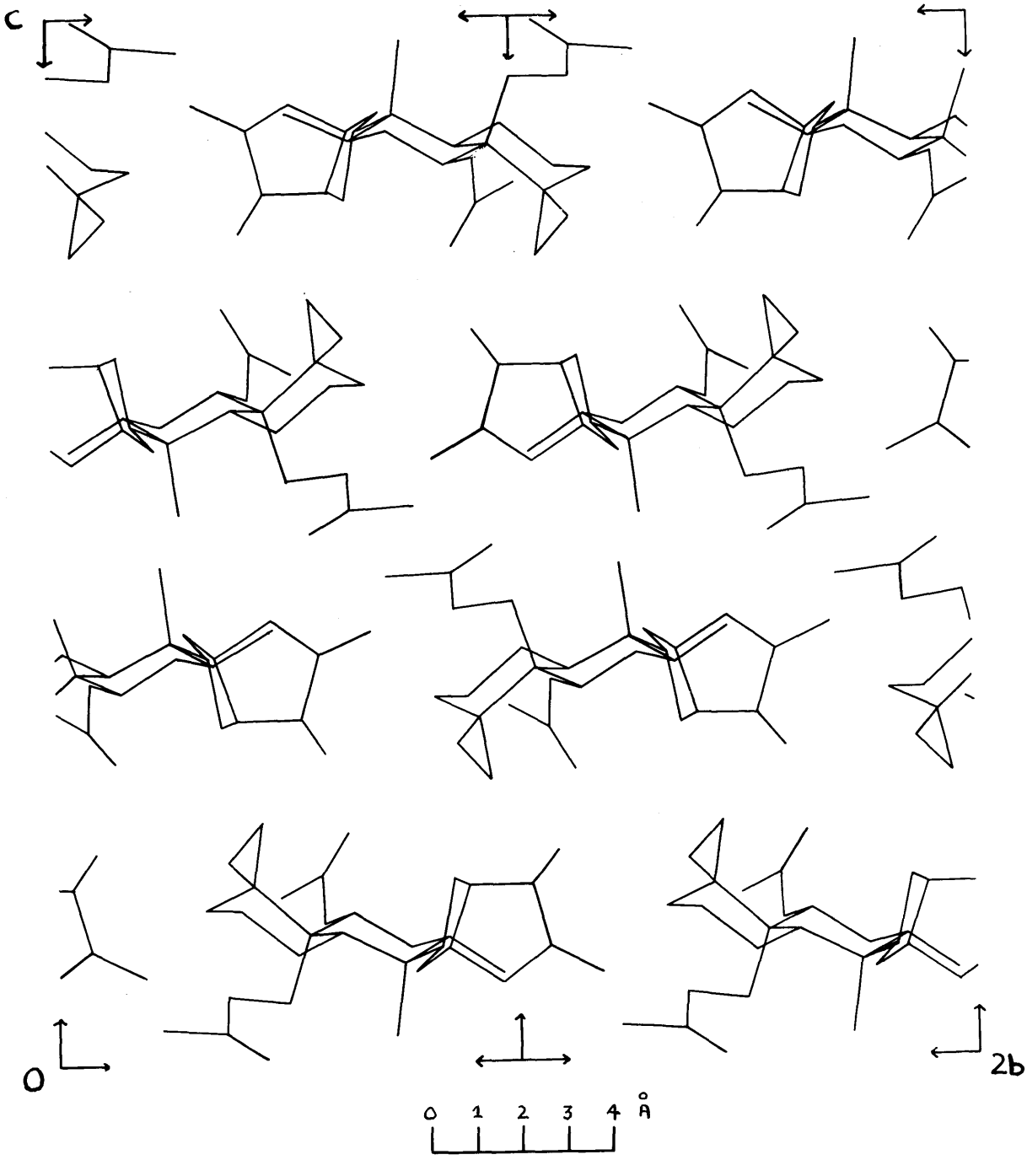


Fig.XIII. Line drawings of the molecular framework projected down the a-axis.

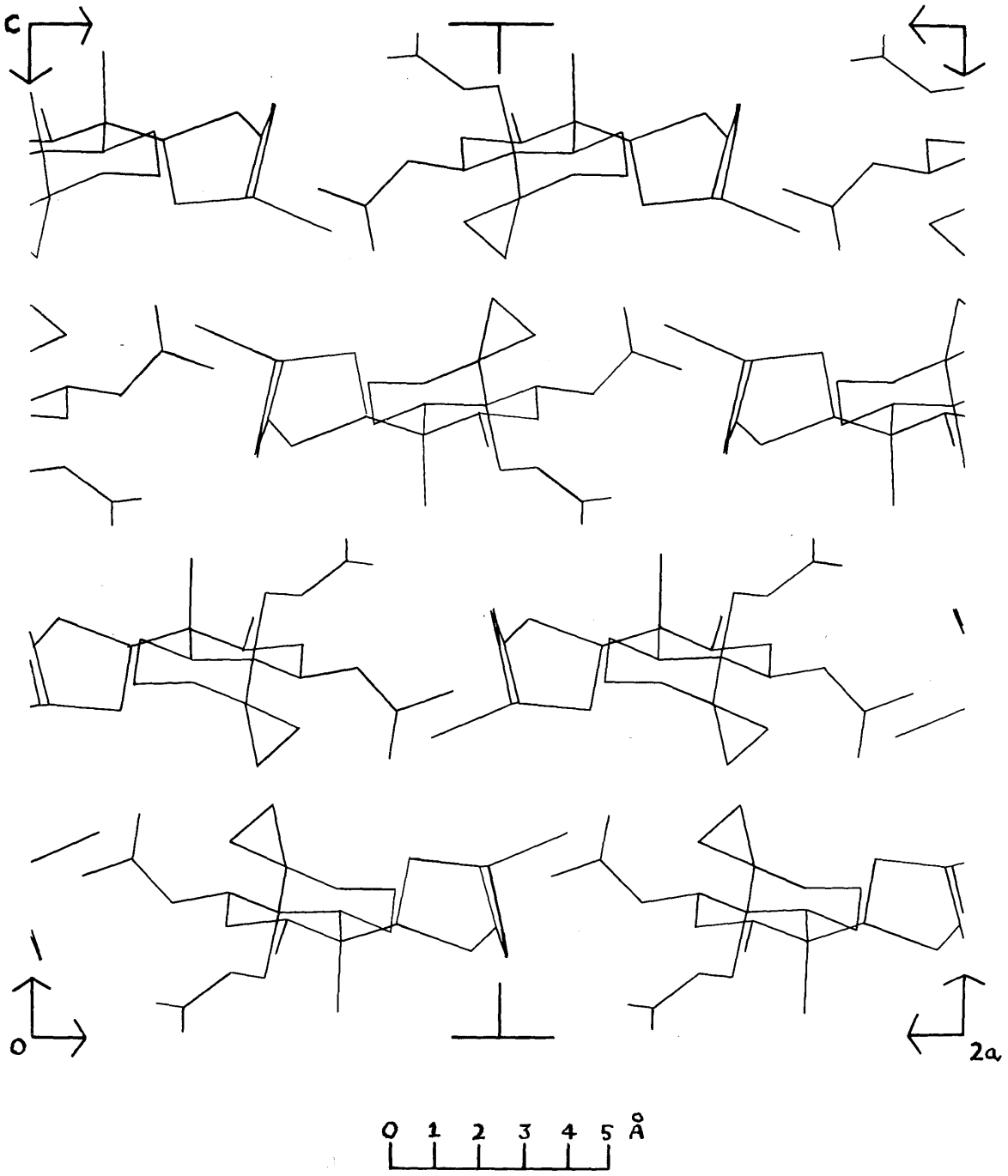


Fig.XIV. Line drawings of the molecular framework projected down the b-axis.

In general, these parameters show a marked tendency for the molecule to vibrate in a direction parallel to the b-axis.

The final values of $|F_o|$, $|F_c|$, and $\alpha(hk\ell)$, giving a discrepancy of 16% are listed in Table XIII. The values of $|F_o|$ and $|F_c|$ are rounded off as integers.

An electron density projection down the a-axis was calculated from the final structure factor output, and is shown in Fig.XV with the sites of atoms marked on it. This map indicates how difficult it would be to solve a structure of this type in projection, as very few of the light atoms are resolved.

In retrospect, a three-dimensional superimposed contour map with sections parallel to $(0,1,0)$ was drawn over the atoms in the molecule from the first Fourier map. This is shown in Fig. XVI. The peak heights of all the atoms on this Fourier map are given in Table XIV. There was no peak corresponding to the position of C(14) on the first Fourier map, but there was a 'diffraction ripple' having similar y- and z- co-ordinates to those of the bromine atom and very near to the position where C(14) was later located. The 'trough' caused by this diffraction effect may well have reduced the genuine peak height due to C(14). If this atom could have been

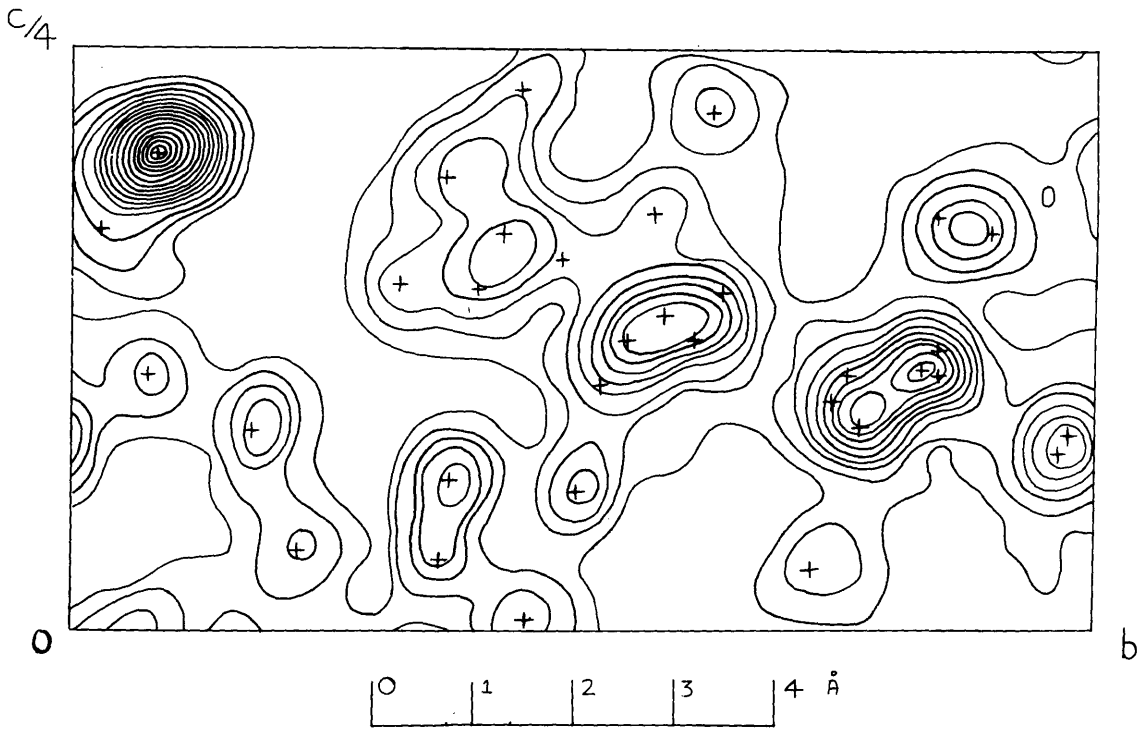


Fig. XV. Electron density projection down the a-axis. The atom sites are marked by crosses. The contour levels are drawn at 2 electrons/Å^2 intervals, the lowest contour representing 2 electrons/Å^2. Around the bromine atom, the contours are drawn at 4 electrons/Å^2 intervals.

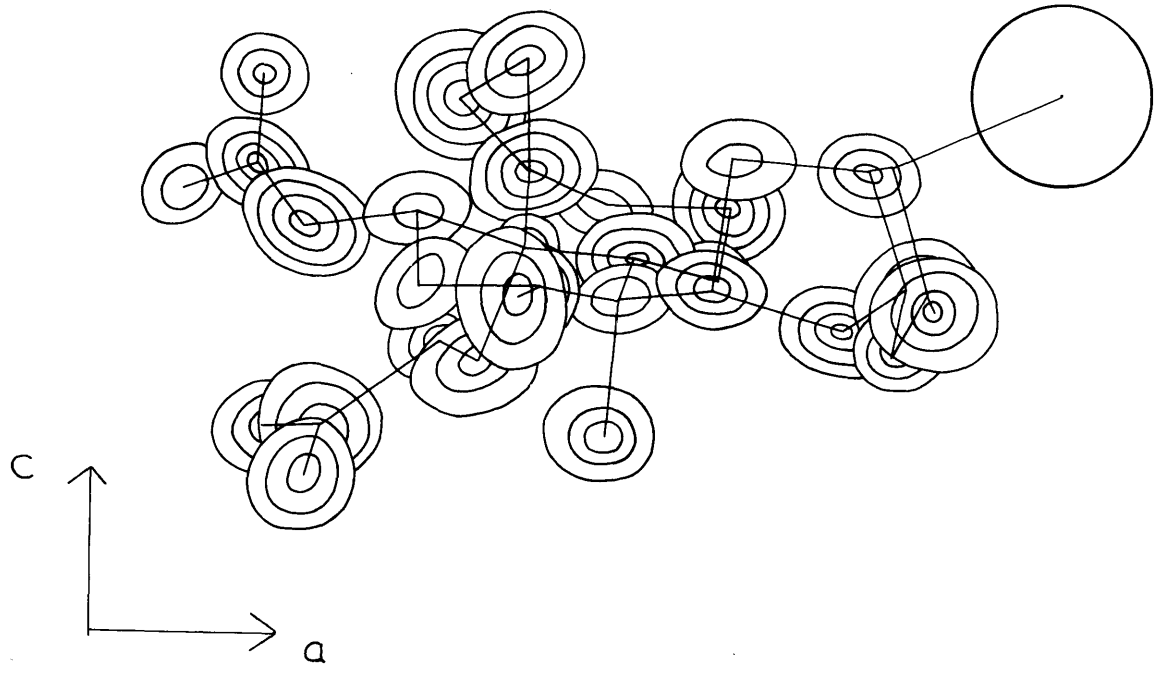


Fig.XVI. The first three-dimensional map, with the peaks representing the various atoms shown on superimposed contour sections parallel to (010). The contours are drawn at levels of 1 electron/$\AA^3$ up to 3 electrons/$\AA^3$, and thereafter at levels of 0.5 electron/$\AA^3$. The zero contour is omitted.

identified at an earlier stage in the analysis, the solution of the structure could well have been achieved much earlier. This effect may also account for the surprising final position of C(14) causing slightly anomalous molecular dimensions in that region of the molecule. Such loss of genuine detail can often occur in the region of a heavy atom, and supports the view that heavy atoms which are ionic in nature, e.g. as in the alkaloids, are more suitable for structure determination. The sums of the ionic radii of anion and cation are then usually sufficient to keep the heavy atom at such a distance that the diffraction effects do not affect the structure to so great an extent.

During the course of the analysis, the scattering curves of Berghuis et al (1955) were used for carbon and oxygen atoms, while that used for bromine was the Thomas-Fermi curve (Internationale Tabellen, 1935). No correction for anomalous dispersion was made.

Barton, Cheung, Cross, Jackman and Martin-Smith (1961) have published the results of their chemical work on clerodin before and after the elucidation of the structure.

TABLE VI.

Atomic Co-ordinates.

	x/a	y/b	z/c
C(1)	-0.2340	-0.4830	0.1046
C(2)	-0.2205	-0.6047	0.1485
C(3)	-0.3459	-0.6827	0.1480
C(4)	-0.4551	-0.5788	0.1694
C(5)	-0.4712	-0.4565	0.1243
C(6)	-0.5782	-0.3591	0.1446
C(7)	-0.5830	-0.2370	0.1098
C(8)	-0.4554	-0.1638	0.1182
C(9)	-0.3393	-0.2520	0.0952
C(10)	-0.3424	-0.3863	0.1262
C(11)	-0.2184	-0.1656	0.1121
C(12)	-0.1913	-0.1412	0.1772
C(13)	-0.0416	-0.1062	0.1705
C(14)	-0.0299	0.0315	0.1697
C(15)	-0.0010	0.0694	0.1088
C(16)	-0.0059	-0.1542	0.1104
C(17)	-0.4860	-0.5576	0.2316
C(18)	-0.5011	-0.5049	0.0585
C(19)	-0.3416	-0.2705	0.0251

- Cont'd -

TABLE VI. Cont'd.

	x/a	y/b	z/c
C(20)	-0.4761	-0.0267	0.0831
C(21)	-0.6762	-0.6400	0.0304
C(22)	-0.7371	-0.7815	0.0345
C(23)	-0.7862	-0.4308	0.1781
C(24)	-0.8913	-0.5203	0.1596
O(1)	-0.5769	-0.6297	0.1945
O(2)	-0.5740	-0.6361	0.0648
O(3)	-0.7226	-0.5540	0.0057
O(4)	-0.6974	-0.4258	0.1338
O(5)	-0.7683	-0.3728	0.2214
O(6)	-0.1050	-0.2260	0.0856
O(7)	0.0193	-0.0360	0.0761
O(8)	-0.0093	0.1830	0.0854
Br	0.1442	0.0828	0.2036

TABLE VII.

Standard Deviations in Atomic Position.

(in Å)

	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$
C(1)	0.031	0.032	0.027
C(2)	0.031	0.028	0.027
C(3)	0.027	0.030	0.026
C(4)	0.030	0.033	0.029
C(5)	0.026	0.025	0.024
C(6)	0.028	0.029	0.027
C(7)	0.031	0.032	0.027
C(8)	0.032	0.030	0.029
C(9)	0.029	0.028	0.024
C(10)	0.027	0.024	0.025
C(11)	0.027	0.030	0.025
C(12)	0.027	0.030	0.026
C(13)	0.028	0.033	0.028
C(14)	0.029	0.030	0.030
C(15)	0.030	0.032	0.026
C(16)	0.028	0.029	0.024
C(17)	0.029	0.033	0.025
C(18)	0.027	0.027	0.025
C(19)	0.033	0.029	0.025
C(20)	0.030	0.033	0.031

-Cont'd-

TABLE VII. (Cont'd)

Standard Deviations in Atomic Position.
(in Å)

	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$
C(21)	0.032	0.032	0.029
C(22)	0.031	0.030	0.026
C(23)	0.029	0.030	0.026
C(24)	0.029	0.031	0.029
O(1)	0.021	0.021	0.018
O(2)	0.019	0.021	0.017
O(3)	0.021	0.021	0.019
O(4)	0.018	0.021	0.017
O(5)	0.020	0.024	0.019
O(6)	0.019	0.019	0.018
O(7)	0.017	0.017	0.018
O(8)	0.018	0.018	0.019
Br	0.004	0.005	0.004

TABLE VIII

Bond Lengths in Å, with standard deviations.

C(1) - C(2) 1.59 ± 0.04	C(11) - O(6) 1.47 ± 0.03
C(1) - C(10) 1.58 ± 0.04	C(12) - C(13) 1.63 ± 0.04
C(2) - C(3) 1.54 ± 0.04	C(13) - C(14) 1.40 ± 0.04
C(3) - C(4) 1.63 ± 0.04	C(13) - C(16) 1.50 ± 0.04
C(4) - C(5) 1.62 ± 0.04	C(14) - C(15) 1.48 ± 0.04
C(4) - C(17) 1.47 ± 0.04	C(14) - Br 2.06 ± 0.03
C(4) - O(1) 1.50 ± 0.04	C(15) - O(7) 1.32 ± 0.03
C(5) - C(6) 1.57 ± 0.04	C(15) - O(8) 1.27 ± 0.03
C(5) - C(10) 1.53 ± 0.04	C(16) - O(6) 1.39 ± 0.03
C(5) - C(18) 1.61 ± 0.04	C(16) - O(7) 1.45 ± 0.03
C(6) - C(7) 1.47 ± 0.04	C(17) - O(1) 1.47 ± 0.04
C(6) - O(4) 1.45 ± 0.03	C(18) - O(2) 1.54 ± 0.03
C(7) - C(8) 1.55 ± 0.04	C(21) - C(22) 1.57 ± 0.04
C(8) - C(9) 1.60 ± 0.04	C(21) - O(2) 1.33 ± 0.04
C(8) - C(20) 1.62 ± 0.04	C(21) - O(3) 1.15 ± 0.04
C(9) - C(10) 1.53 ± 0.04	C(23) - C(24) 1.49 ± 0.04
C(9) - C(11) 1.59 ± 0.04	C(23) - O(4) 1.38 ± 0.03
C(9) - C(19) 1.61 ± 0.04	C(23) - O(5) 1.17 ± 0.04
C(11) - C(12) 1.53 ± 0.04	

TABLE IX.

Bond Angles.

C(10)-C(1) -C(2)	110°	C(7) -C(8) -C(20)	103°
C(1) -C(2) -C(3)	108°	C(9) -C(8) -C(20)	115°
C(2) -C(3) -C(4)	106°	C(8) -C(9) -C(10)	109°
C(3) -C(4) -C(5)	112°	C(8) -C(9) -C(11)	103°
C(3) -C(4) -C(17)	123°	C(8) -C(9) -C(19)	112°
C(3) -C(4) -O(1)	120°	C(10)-C(9) -C(11)	113°
C(5) -C(4) -C(17)	119°	C(10)-C(9) -C(19)	111°
C(5) -C(4) -O(1)	115°	C(11)-C(9) -C(19)	108°
C(17)-C(4) -O(1)	59°	C(1) -C(10)-C(5)	110°
C(4) -C(5) -C(6)	112°	C(1) -C(10)-C(9)	113°
C(4) -C(5) -C(10)	104°	C(5) -C(10)-C(9)	115°
C(4) -C(5) -C(18)	112°	C(9) -C(11)-C(12)	118°
C(6) -C(5) -C(10)	110°	C(9) -C(11)-O(6)	109°
C(6) -C(5) -C(18)	109°	C(12)-C(11)-O(6)	108°
C(10)-C(5) -C(18)	110°	C(11)-C(12)-C(13)	97°
C(5) -C(6) -C(7)	113°	C(12)-C(13)-C(14)	108°
C(5) -C(6) -O(4)	106°	C(12)-C(13)-C(16)	105°
C(7) -C(6) -O(4)	106°	C(14)-C(13)-C(16)	107°
C(6) -C(7) -C(8)	108°	C(13)-C(14)-C(15)	107°
C(7) -C(8) -C(9)	111°	C(13)-C(14)-Br	109°

- Cont'd -

TABLE IX. (Cont'd)

Bond Angles.

C(15) - C(14) - Br	96°
C(14) - C(15) - O(7)	111°
C(14) - C(15) - O(8)	128°
O(7) - C(15) - O(8)	120°
C(13) - C(16) - O(6)	111°
C(13) - C(16) - O(7)	106°
O(6) - C(16) - O(7)	110°
C(4) - C(17) - O(1)	61°
C(5) - C(18) - O(2)	106°
C(22) - C(21) - O(2)	109°
C(22) - C(21) - O(3)	123°
O(2) - C(21) - O(3)	128°
C(24) - C(23) - O(4)	109°
C(24) - C(23) - O(5)	132°
O(4) - C(23) - O(5)	120°
C(18) - O(2) - C(21)	112°
C(6) - O(3) - C(23)	119°

TABLE X.

Some Intramolecular
Non-bonded Contacts (in Å).

C(1)	.... C(4)	2.93	C(12)	....C(15)	3.32
C(1)	.... C(11)	3.22	C(12)	....C(20)	3.87
C(1)	.... C(12)	3.86	C(12)	....O(7)	3.38
C(1)	.... O(6)	2.97	C(14)	....O(6)	3.33
C(2)	.... C(5)	3.09	C(15)	....O(6)	3.23
C(3)	.... C(10)	3.04	C(18)	....C(19)	3.01
C(4)	.... O(2)	2.76	C(18)	....O(1)	3.44
C(5)	.... C(8)	2.97	C(18)	....O(3)	2.68
C(6)	.... C(9)	2.97	C(18)	....O(4)	2.81
C(7)	.... C(10)	2.98	C(19)	....C(20)	3.14
C(7)	.... O(5)	3.49	C(19)	....O(6)	2.89
C(8)	.... C(12)	3.10	C(23)	....O(1)	3.01
C(8)	.... O(6)	3.82	C(24)	....O(3)	3.95
C(10)	.... C(12)	3.17	O(1)	....O(2)	2.96
C(10)	.... O(6)	3.12	O(1)	....O(4)	2.79
C(11)	.... C(14)	3.11	O(1)	....O(5)	3.35
C(11)	.... C(15)	3.31	O(2)	....O(4)	2.95
C(11)	.... C(20)	3.13	O(3)	....O(4)	3.21
C(11)	.... O(7)	2.95	O(8)	....Br	3.31

TABLE XI.

Intermolecular Bond Lengths (< 4 Å).

The Roman Numerals refer to:

I. x, 1+y, z	IV. $\bar{x}$, $\frac{1}{2}$+y, $\frac{1}{2}$-z
II. 1+x, y, z	V. -1-x, $\frac{1}{2}$+y, $\frac{1}{2}$-z
III. 1+x, 1+y, z	VI. $\frac{1}{2}$+x, $-\frac{1}{2}$-y, $\bar{z}$

O(7) ....C(18)^{VI}	3.11	O(7) ....C(21)^{VI}	3.65
O(8) ....C(22)^{III}	3.12	O(8) ....C(24)^{III}	3.67
O(8) ....C(21)^{VI}	3.21	O(6) ....O(3)^{VI}	3.73
O(7) ....O(3) ^{VI}	3.29	C(15)....C(21^{VI}	3.75
O(8) ....O(3)^{VI}	3.33	O(5) ....C(3)^{V}	3.75
O(7) ....C(19)^{VI}	3.36	O(8) ....C(18)^{VI}	3.75
O(8) ....C(2)^{I}	3.41	O(6) ....C(19)^{VI}	3.76
C(14)....O(5)^{V}	3.41	O(7) ....C(22)^{III}	3.76
C(20)....O(3)^{VI}	3.45	O(8) ....C(22)^{VI}	3.78
C(11)....O(3)^{VI}	3.49	O(7) ....O(2)^{VI}	3.79
C(15)....O(3)^{VI}	3.52	C(12)....O(1)^{V}	3.82
O(8) ....O(2)^{VI}	3.53	C(1) ....C(24)^{II}	3.85
C(15)....C(22)^{III}	3.58	C(15)....C(18)^{VI}	3.87
C(2).....C(24)^{II}	3.59	C(20)....C(22)^{I}	3.87
C(12)....O(5)^{V}	3.59	Br ....C(12)^{IV}	3.93
C(19)....O(3)^{VI}	3.59	C(12)....C(23)^{V}	3.94
C(16)....C(19)^{VI}	3.63	C(16)....C(23)^{II}	3.95
C(8) ....C(17)^{V}	3.64	Br ....C(2)^{IV}	3.95
		C(13)....O(5)^{V}	3.96

TABLE XII.

Final Anisotropic
Thermal Parameters ($b_{ij} \times 10^5$).

	b_{11}	b_{22}	b_{33}	b_{12}	b_{23}	b_{13}
C(1)	521	1277	307	-445	137	-83
C(2)	1257	1269	330	-772	-182	14
C(3)	592	2100	323	-706	-189	45
C(4)	1081	1559	358	-466	-86	-460
C(5)	884	1180	231	-840	38	-225
C(6)	777	1751	312	-1688	-234	-200
C(7)	1118	1988	322	-490	299	55
C(8)	1071	1726	183	-505	-384	81
C(9)	712	1409	239	254	75	-152
C(10)	697	1003	287	-409	122	27
C(11)	588	1888	240	-530	-168	89
C(12)	875	1894	231	198	349	-40
C(13)	956	2101	279	35	-88	-12
C(14)	1014	1680	321	-427	-130	-78
C(15)	1461	1792	287	-2277	-94	122
C(16)	1143	1620	198	-120	-397	-14
C(17)	938	1901	285	386	525	484
C(18)	747	1383	221	-1432	-200	-38

- Cont'd -

TABLE XII. (Cont'd)

Final Anisotropic

Thermal Parameters (b_{ij} x 10^5).

	b_{11}	b_{22}	b_{33}	b_{12}	b_{23}	b_{13}
C(19)	1163	1741	227	-634	217	-90
C(20)	909	1918	426	571	303	76
C(21)	1168	1484	342	-169	186	-36
C(22)	1398	1531	301	-2260	-404	83
C(23)	1000	1528	288	241	67	4
C(24)	611	2225	358	555	-304	-3
O(1)	1270	2032	264	673	206	-44
O(2)	1036	1871	260	-633	78	-289
O(3)	1301	2023	327	141	467	290
O(4)	972	1783	288	-610	297	-22
O(5)	1087	2594	398	-488	-401	570
O(6)	1071	1255	304	-381	81	-86
O(7)	674	1060	363	115	47	408
O(8)	1074	985	414	235	256	-434
Br	1928	2525	339	-1770	-44	-318

TABLE XIII. Values of $|s|$, $|s|^2$ and α.

h	k	ℓ	F_o	F_o^2	α
0	0	2	39	60	180
		4	113	115	180
		6	27	11	0
		8	47	51	180
		10	113	113	0
		12	37	37	180
		14	14	4	0
		16	12	7	180
		18	9	2	0
		20	25	26	180
		24	10	3	0
0	1	1	9	2	90
		3	43	40	90
		5	7	15	270
		7	152	151	90
		9	72	70	90
		11	9	11	270
		13	112	122	270
		15	54	53	270
		17	10	4	270
		19	11	2	270
		21	11	11	270
		23	11	16	270
		25	9	10	90
		27	7	4	270
0	2	0	107	120	0
		2	93	40	180
		4	78	80	180
		6	78	93	0
		8	7	1	180
		10	44	52	0
		12	23	18	0
		14	9	14	180
		16	23	24	0
		18	8	2	0
		20	9	7	180
		22	7	7	0
		24	7	3	180
0	3	1	44	44	90
		3	44	46	90
		5	44	46	90
		7	44	46	90
		9	44	46	90
		11	44	46	90
		13	44	46	90
		15	44	46	90
		17	44	46	90
		19	44	46	90
		21	44	46	90
		23	44	46	90
		25	44	46	90
		27	44	46	90
0	4	0	44	52	0
		2	44	46	90
		4	44	46	90
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		3	44	46	90
		5

TABLE XIV.

The values of the Maxima at the position of each Atom in the first Fourier (F_o) Synthesis(in electrons/$\mathring{A}^3$).

C(1)	2.92	C(17)	3.07
C(2)	3.68	C(18)	3.10
C(3)	2.69	C(19)	3.04
C(4)	3.62	C(20)	3.07
C(5)	3.03	C(21)	3.10
C(6)	2.80	C(22)	3.41
C(7)	2.98	C(23)	3.74
C(8)	3.27	C(24)	2.83
C(9)	2.91	O(1)	3.78
C(10)	3.53	O(2)	3.09
C(11)	3.03	O(3)	3.39
C(12)	2.89	O(4)	3.61
C(13)	3.10	O(5)	3.12
C(14)	-	O(6)	3.67
C(15)	2.35	O(7)	3.67
C(16)	3.02	O(8)	3.84

PART II.

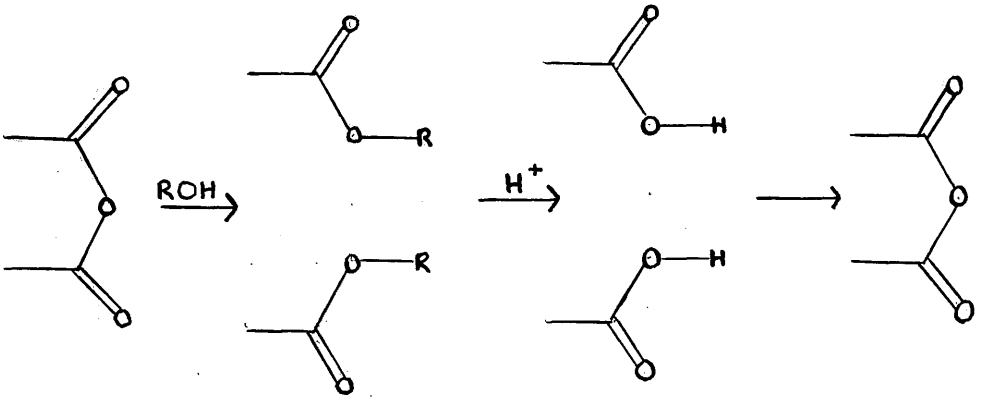
The Structure of Byssochlamic Acid:

The X-ray Analysis of a p-bromophenylhydrazine Derivative.

The Structure of Byssochlamic Acid: The X-ray Analysis of a p-bromophenylhydrazine Derivative.

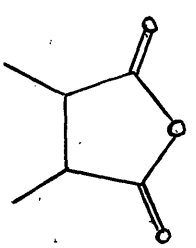
Introduction:

In 1933, Olliver and Smith described a new Ascomycete, Byssochlamys fulva which causes spoilage in processed fruits and is very difficult to destroy. A study of the metabolic products formed when Byssochlamys fulva is grown on a synthetic medium with glucose as the sole source of carbon was undertaken by Raistrick and Smith (1933), who were able to isolate a new and specific mould product, $C_{18}H_{20}O_6$ (m.p. 163.5°), which was toxic to mice. This substance titrates as a tetrabasic acid, so they named it byssochlamic acid. Raistrick and Smith found that byssochlamic acid gave salts of the type $C_{18}H_{20}O_8R_4$, acidification giving $C_{18}H_{24}O_8$ before loss of two molecules of water to regenerate byssochlamic acid. This pattern suggests the presence of two anhydride groups

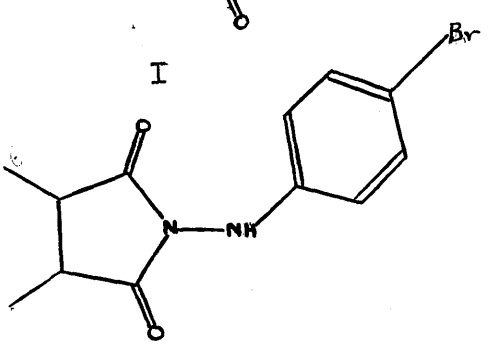


Wijkman (1931) described a mould product, glaucanic acid, also of formula $C_{18}H_{20}O_6$, which titrates as a tetrabasic acid. This fact is mentioned because the closely-related glauconic acid was to play a part in the elucidation of the structure of byssochlamic acid.

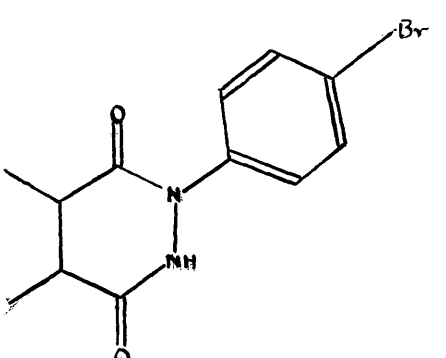
Barton (1960) had shown that the anhydride groups existed as five-membered rings (I) and he was able to provide crystals of a derivative of byssochlamic acid formed by reaction with p-bromophenylhydrazine in chloroform solution, the point of attack being the five-membered ring. Barton suggested alternative structures (II and III) for this part of the molecule.



I



II



III

When he sent the crystals, Barton was unable to tell if both anhydride rings or only one had reacted with p-bromophenylhydrazine. The preliminary X-ray work showed that both rings had been attached and that the molecular formula of the derivative was $C_{30}H_{30}O_4N_4Br_2$, a fact later confirmed by Barton. The derivative can be called byssochlamic acid bis-p-bromophenylhydrazide or N,N'-bis-(p-bromoanilino) byssochlamic acid diimide.

Experimental:

Crystal Data.

Molecular Formula	$C_{30}H_{30}O_4N_4Br_2$
Molecular Weight	669.8
Melting Point	164 - 166°C.
Density (calc.)	1.524 gm/cc.
Density (meas.)	1.505 gm./cc.
Crystal System	Tetragonal
a	10.07 Å.
c	57.61 Å.
Unit Cell Volume	5841.9×10^{-24} cc.
No. of molecules/cell	8
Absent Spectra	h00(0k0) when h(k) is odd. 00ℓ when $\ell \neq 4n$.
Space Group	$P4_12_12$ (D_4^4) or its enantiomorph $P4_32_12$ (D_4^8).
Absorption Coefficient for X-rays:	
($\lambda = 1.542$) μ	40.3 cm.$^{-1}$
F (000)	2720

Rotation, oscillation, Weissenberg, and precession photographs were taken with CuK_α radiation ($\lambda = 1.542$ Å) and MoK_α radiation ($\lambda = 0.7107$ Å). The cell dimensions were obtained from rotation and precession photographs.

The intensities were collected by zero layer and equi-inclination Weissenberg photographs obtained by rotating the crystal about one of the 10.07 Å axes. The intensities were estimated visually, corrected for Lorentz, polarisation, and rotation factors and reduced to structure amplitudes by the mosaic crystal formula. As the crystal belongs to the tetragonal system, most reflexions have symmetrically-equivalent reflexions occurring on different zones obtained by rotation about the same axis. The occurrence of such reflexions provided the basis for interzonal scaling, all structure amplitudes being scaled relative to those on the zero layer. Absolute scaling was achieved at a later stage by comparison with the calculated structure amplitudes. It was realised that the atoms in the structure would have high temperature factors, as the data faded out rapidly above $\sin\theta = 0.6$. The density was measured by flotation of a crystal in a mixture of saturated zinc chloride solution and water.

In all, 1,190 independent structure amplitudes were obtained.

TABLE I(a).

The vectors to be expected in the space group $P4_12_12$ between symmetrically related atoms.

ATOMIC POSITIONS	x y z	y x $\bar{z}$	$\bar{x}$ $\bar{y}$ $\frac{1}{2}+z$	$\bar{y}$ $\bar{x}$ $\frac{1}{2}-z$	$\frac{1}{2}-y$ $\frac{1}{2}+x$ $\frac{1}{4}+z$	$\frac{1}{2}-x$ $\frac{1}{2}+y$ $\frac{1}{4}-z$	$\frac{1}{2}+y$ $\frac{1}{2}-x$ $\frac{3}{4}+z$	$\frac{1}{2}+x$ $\frac{1}{2}-y$ $\frac{3}{4}-z$
x y z	—	$x-y$ $y-x$ $2z$	$2x$ $2y$ $\frac{1}{2}$	$x+y$ $y+x$ $\frac{1}{2}+2z$	$\frac{1}{2}+x-y$ $\frac{1}{2}+x+y$ $\frac{3}{4}$	$\frac{1}{2}+2x$ $\frac{1}{2}$ $\frac{3}{4}+2z$	$\frac{1}{2}+x-y$ $\frac{1}{2}+y+x$ $\frac{1}{4}$	$\frac{1}{2}$ $\frac{1}{2}+2y$ $\frac{1}{4}+2z$
y x $\bar{z}$	$y-x$ $x-y$ $-2z$	—	$y+x$ $x+y$ $\frac{1}{2}-2z$	$2y$ $2x$ $\frac{1}{2}$	$\frac{1}{2}+2y$ $\frac{1}{2}$ $\frac{3}{4}-2z$	$\frac{1}{2}+y+x$ $\frac{1}{2}+x-y$ $\frac{3}{4}$	$\frac{1}{2}$ $\frac{1}{2}+2x$ $\frac{1}{4}-2z$	$\frac{1}{2}+y-x$ $\frac{1}{2}+x+y$ $\frac{1}{4}$
$\bar{x}$ $\bar{y}$ $\frac{1}{2}+z$	$-2x$ $-2y$ $\frac{1}{2}$	$-x-y$ $-y-x$ $\frac{1}{2}+2z$	—	$-x+y$ $-y+x$ $2z$	$\frac{1}{2}-x+y$ $\frac{1}{2}-y-x$ $\frac{1}{4}$	$\frac{1}{2}$ $\frac{1}{2}-2y$ $\frac{1}{4}+2z$	$\frac{1}{2}-x-y$ $\frac{1}{2}+x-y$ $\frac{3}{4}$	$\frac{1}{2}-2x$ $\frac{1}{2}$ $\frac{3}{4}+2z$
$\bar{y}$ $\bar{x}$ $\frac{1}{2}-z$	$-y-x$ $-x-y$ $\frac{1}{2}-2z$	$-2y$ $-2x$ $\frac{1}{2}$	$-y+x$ $-x+y$ $-2z$	—	$\frac{1}{2}$ $\frac{1}{2}-2x$ $\frac{1}{4}-2z$	$\frac{1}{2}-y+x$ $\frac{1}{2}-x-y$ $\frac{1}{4}$	$\frac{1}{2}-2y$ $\frac{1}{2}$ $\frac{3}{4}-2z$	$\frac{1}{2}-y-x$ $\frac{1}{2}-x+y$ $\frac{3}{4}$
$\frac{1}{2}-y$ $\frac{1}{2}+x$ $\frac{1}{4}+z$	$\frac{1}{2}-y-x$ $\frac{1}{2}+x-y$ $\frac{1}{4}$	$\frac{1}{2}-2y$ $\frac{1}{2}$ $\frac{1}{4}+2z$	$\frac{1}{2}-y+x$ $\frac{1}{2}+x+y$ $\frac{3}{4}$	$\frac{1}{2}$ $\frac{1}{2}+2x$ $\frac{3}{4}+2z$	—	$-y+x$ $x-y$ $2z$	$-2y$ $2x$ $\frac{1}{2}$	$-y-x$ $x+y$ $\frac{1}{2}+2z$
$\frac{1}{2}-x$ $\frac{1}{2}+y$ $\frac{1}{4}-z$	$\frac{1}{2}-2x$ $\frac{1}{2}$ $\frac{1}{4}-2z$	$\frac{1}{2}-x-y$ $\frac{1}{2}+y-x$ $\frac{1}{4}$	$\frac{1}{2}$ $\frac{1}{2}+2y$ $\frac{3}{4}-2z$	$\frac{1}{2}-x+y$ $\frac{1}{2}+y+x$ $\frac{3}{4}$	$-x+y$ $y-x$ $-2z$	—	$-x-y$ $y+x$ $\frac{1}{2}-2z$	$-2x$ $2y$ $\frac{1}{2}$
$\frac{1}{2}+y$ $\frac{1}{2}-x$ $\frac{3}{4}+z$	$\frac{1}{2}+y-x$ $\frac{1}{2}-x-y$ $\frac{3}{4}$	$\frac{1}{2}$ $\frac{1}{2}-2x$ $\frac{3}{4}+2z$	$\frac{1}{2}+y+x$ $\frac{1}{2}-x+y$ $\frac{1}{4}$	$\frac{1}{2}+2y$ $\frac{1}{2}$ $\frac{1}{4}+2z$	$2y$ $-2x$ $\frac{1}{2}$	$y+x$ $-x-y$ $\frac{1}{2}+2z$	—	$y-x$ $-x+y$ $2z$
$\frac{1}{2}+x$ $\frac{1}{2}-y$ $\frac{3}{4}-z$	$\frac{1}{2}$ $\frac{1}{2}-2y$ $\frac{3}{4}-2z$	$\frac{1}{2}+x-y$ $\frac{1}{2}-y-x$ $\frac{3}{4}$	$\frac{1}{2}+2x$ $\frac{1}{2}$ $\frac{1}{4}-2z$	$\frac{1}{2}+x+y$ $\frac{1}{2}-y+x$ $\frac{1}{4}$	$x+y$ $-y-x$ $\frac{1}{2}-2z$	$2x$ $-2y$ $\frac{1}{2}$	$x-y$ $-y+x$ $-2z$	—

TABLE I(b).

The vectors to be expected in the space group $P4_12_12$ between two atoms not related by symmetry. In the full unit cell, there will be twice the number of vectors as shown in this table, on account of the centre of symmetry of the Patterson function.

Br_2 \ Br_1	x_1 y_1 z_1	y_1 x_1 $\bar{z}_1$	$\bar{x}_1$ $\bar{y}_1$ $\frac{1}{2}+z_1$	$\bar{y}_1$ $\bar{x}_1$ $\frac{1}{2}-z_1$	$\frac{1}{2}-y_1$ $\frac{1}{2}+x_1$ $\frac{1}{4}+z_1$	$\frac{1}{2}-x_1$ $\frac{1}{2}+y_1$ $\frac{1}{4}-z_1$	$\frac{1}{2}+y_1$ $\frac{1}{2}-x_1$ $\frac{3}{4}+z_1$	$\frac{1}{2}+x_1$ $\frac{1}{2}-y_1$ $\frac{3}{4}-z_1$
x_2 y_2 z_2	x_1-x_2 y_1-y_2 z_1-z_2	y_1-x_2 x_1-y_2 $-z_1-z_2$	$-x_1-x_2$ $-y_1-y_2$ $\frac{1}{2}+z_1-z_2$	$-y_1-x_2$ $-x_1-y_2$ $\frac{1}{2}-z_1-z_2$	$\frac{1}{2}-y_1-x_2$ $\frac{1}{2}+x_1-y_2$ $\frac{1}{4}+z_1-z_2$	$\frac{1}{2}-x_1-x_2$ $\frac{1}{2}+y_1-y_2$ $\frac{1}{4}-z_1-z_2$	$\frac{1}{2}+y_1-x_2$ $\frac{1}{2}-x_1-y_2$ $\frac{3}{4}+z_1-z_2$	$\frac{1}{2}+x_1-x_2$ $\frac{1}{2}-y_1-y_2$ $\frac{3}{4}-z_1-z_2$
y_2 x_2 $\bar{z}_2$	x_1-y_2 y_1-x_2 z_1+z_2	y_1-y_2 x_1-x_2 $-z_1+z_2$	$-x_1-y_2$ $-y_1-x_2$ $\frac{1}{2}+z_1+z_2$	$-y_1-y_2$ $-x_1-x_2$ $\frac{1}{2}-z_1+z_2$	$\frac{1}{2}-y_1-y_2$ $\frac{1}{2}+x_1-x_2$ $\frac{1}{4}+z_1+z_2$	$\frac{1}{2}-x_1-y_2$ $\frac{1}{2}+y_1-x_2$ $\frac{1}{4}-z_1+z_2$	$\frac{1}{2}+y_1-y_2$ $\frac{1}{2}-x_1-x_2$ $\frac{3}{4}+z_1+z_2$	$\frac{1}{2}+x_1-y_2$ $\frac{1}{2}-y_1-x_2$ $\frac{3}{4}-z_1+z_2$
$\bar{x}_2$ $\bar{y}_2$ $\frac{1}{2}+z_2$	x_1+x_2 y_1+y_2 $\frac{1}{2}+z_1-z_2$	y_1+x_2 x_1+y_2 $\frac{1}{2}-z_1-z_2$	$-x_1+x_2$ $-y_1+y_2$ z_1-z_2	$-y_1+x_2$ $-x_1+y_2$ $-z_1-z_2$	$\frac{1}{2}-y_1+x_2$ $\frac{1}{2}+x_1+y_2$ $\frac{3}{4}+z_1-z_2$	$\frac{1}{2}-x_1+x_2$ $\frac{1}{2}+y_1+y_2$ $\frac{3}{4}-z_1-z_2$	$\frac{1}{2}+y_1+x_2$ $\frac{1}{2}-x_1+y_2$ $\frac{1}{4}+z_1-z_2$	$\frac{1}{2}+x_1+x_2$ $\frac{1}{2}-y_1+y_2$ $\frac{1}{4}-z_1-z_2$
$\bar{y}_2$ $\bar{x}_2$ $\frac{1}{2}-z_2$	x_1+y_2 y_1+x_2 $\frac{1}{2}+z_1+z_2$	y_1+y_2 x_1+x_2 $\frac{1}{2}-z_1+z_2$	$-x_1+y_2$ $-y_1+x_2$ z_1+z_2	$-y_1+y_2$ $-x_1+x_2$ $-z_1+z_2$	$\frac{1}{2}-y_1+y_2$ $\frac{1}{2}+x_1+x_2$ $\frac{3}{4}+z_1+z_2$	$\frac{1}{2}-x_1+y_2$ $\frac{1}{2}+y_1+x_2$ $\frac{3}{4}-z_1+z_2$	$\frac{1}{2}+y_1+y_2$ $\frac{1}{2}-x_1+x_2$ $\frac{1}{4}+z_1+z_2$	$\frac{1}{2}+x_1+y_2$ $\frac{1}{2}-y_1+x_2$ $\frac{1}{4}-z_1+z_2$
$\frac{1}{2}-y_2$ $\frac{1}{2}+x_2$ $\frac{1}{4}+z_2$	$\frac{1}{2}+x_1+y_2$ $\frac{1}{2}+y_1-x_2$ $\frac{3}{4}+z_1-z_2$	$\frac{1}{2}+y_1+y_2$ $\frac{1}{2}+x_1-x_2$ $\frac{3}{4}-z_1-z_2$	$\frac{1}{2}-x_1+y_2$ $\frac{1}{2}-y_1-x_2$ $\frac{1}{4}+z_1-z_2$	$\frac{1}{2}-y_1+y_2$ $\frac{1}{2}-x_1-x_2$ $\frac{1}{4}-z_1-z_2$	$-y_1+y_2$ x_1-x_2 z_1-z_2	$-x_1+y_2$ y_1-x_2 $-z_1-z_2$	y_1+y_2 $-x_1-x_2$ $\frac{1}{2}+z_1-z_2$	x_1+y_2 $-y_1-x_2$ $\frac{1}{2}-z_1-z_2$
$\frac{1}{2}-x_2$ $\frac{1}{2}+y_2$ $\frac{1}{4}-z_2$	$\frac{1}{2}+x_1+x_2$ $\frac{1}{2}+y_1-y_2$ $\frac{3}{4}+z_1+z_2$	$\frac{1}{2}+y_1+x_2$ $\frac{1}{2}+x_1-y_2$ $\frac{3}{4}-z_1+z_2$	$\frac{1}{2}-x_1+x_2$ $\frac{1}{2}-y_1-y_2$ $\frac{1}{4}+z_1+z_2$	$\frac{1}{2}-y_1+x_2$ $\frac{1}{2}-x_1-y_2$ $\frac{1}{4}-z_1+z_2$	$-y_1+x_2$ x_1-y_2 z_1+z_2	$-x_1+x_2$ y_1-y_2 $-z_1+z_2$	y_1+x_2 $-x_1-y_2$ $\frac{1}{2}+z_1+z_2$	x_1+x_2 $-y_1-y_2$ $\frac{1}{2}-z_1+z_2$
$\frac{1}{2}+y_2$ $\frac{1}{2}-x_2$ $\frac{3}{4}+z_2$	$\frac{1}{2}+x_1-y_2$ $\frac{1}{2}+y_1+x_2$ $\frac{1}{4}+z_1-z_2$	$\frac{1}{2}+y_1-y_2$ $\frac{1}{2}+x_1+x_2$ $\frac{1}{4}-z_1-z_2$	$\frac{1}{2}-x_1-y_2$ $\frac{1}{2}-y_1+x_2$ $\frac{3}{4}+z_1-z_2$	$\frac{1}{2}-y_1-y_2$ $\frac{1}{2}-x_1+x_2$ $\frac{3}{4}-z_1-z_2$	$-y_1-y_2$ x_1+x_2 $\frac{1}{2}+z_1-z_2$	$-x_1-y_2$ y_1+x_2 $\frac{1}{2}-z_1-z_2$	y_1-y_2 $-x_1+x_2$ z_1-z_2	x_1-y_2 $-y_1+x_2$ $-z_1-z_2$
$\frac{1}{2}+x_2$ $\frac{1}{2}-y_2$ $\frac{3}{4}-z_2$	$\frac{1}{2}+x_1-x_2$ $\frac{1}{2}+y_1+y_2$ $\frac{1}{4}+z_1+z_2$	$\frac{1}{2}+y_1-x_2$ $\frac{1}{2}+x_1+y_2$ $\frac{1}{4}-z_1+z_2$	$\frac{1}{2}-x_1-x_2$ $\frac{1}{2}-y_1+y_2$ $\frac{3}{4}+z_1+z_2$	$\frac{1}{2}-y_1-x_2$ $\frac{1}{2}-x_1+y_2$ $\frac{3}{4}-z_1+z_2$	$-y_1-x_2$ x_1+y_2 $\frac{1}{2}+z_1+z_2$	$-x_1-x_2$ y_1+y_2 $\frac{1}{2}-z_1+z_2$	y_1-x_2 $-x_1+y_2$ z_1+z_2	x_1-x_2 $-y_1+y_2$ $-z_1+z_2$

Structure Determination:

I. The Determination of the Heavy Atom Positions.

The expression for the Patterson function of a crystal having the point group 422 is:

$$P(UVW) = {}^{8}/_{V_c} \sum_{0}^{\infty} \sum_{0}^{\infty} \sum_{0}^{\infty} |F(hk\ell)|^2 \cos 2\pi hU \cos 2\pi kV \cos 2\pi \ell W$$

Interpretation of the map of this function will be complicated by the high symmetry of the tetragonal system and by the presence of two heavy atoms in the asymmetric unit of the cell. Not only will each of the heavy atoms in the asymmetric unit be represented in the map by a set of vectors corresponding to the basic vector set of the space group, but there will also be peaks due to vectors between heavy atoms not related by symmetry tending to complicate the map. In the full three-dimensional Patterson synthesis there will be fifty six vectors between each set of symmetrically related bromine atoms, and one hundred and thirty two vectors between non-symmetry related bromine atoms (Table I). On account of the symmetry of the Patterson function it is only necessary to consider six peaks due to vectors between each set of symmetrically related bromine atoms and eight peaks due to vectors between non-symmetrically related bromine atoms. These are shown in Table II.

TABLE II.

Vectors to be considered

in Asymmetric Unit of Patterson Map.

Vector	Co-ordinate Found U	V	W	P(UVW) (Arbitrary Units)
$\frac{1}{2}-2x_1, \frac{1}{2}, \frac{1}{4}-2z_1$	0.24,	0.50,	0.18	9.5
$\frac{1}{2}-2y_1, \frac{1}{2}.\frac{1}{4}+2z_1$	0.26,	0.50,	0.31	5.8
$2x_1$, $2y_1$, $\frac{1}{2}$	0.28,	0.27,	0.50	7.6
$\frac{1}{2}-x_1+y_1, \frac{1}{2}-y_1-x_1, \frac{1}{4}$	0.48,	0.23,	0.25	11.4
y_1+x_1, $x_1+y_1, \frac{1}{2}-2z_1$	0.26,	0.26,	0.06	2.8
$y_1-x_1, y_1-x_1, 2z_1$	0.04,	0.04,	0.44	19.0
$\frac{1}{2}-2x_2, \frac{1}{2}, \frac{1}{4}-2z_2$	0.43,	0.50,	0.21	6.8
$\frac{1}{2}-2y_2, \frac{1}{2}, \frac{1}{4}+2z_2$	0.23,	0.50,	0.29	7.5
$2x_2$, $2y_2$, $\frac{1}{2}$	0.07,	0.24,	0.50	8.8
$\frac{1}{2}-x_2+y_2, \frac{1}{2}-y_2-x_2, \frac{1}{4}$	0.16,	0.10,	0.25	5.1
$y_2+x_2, x_2+y_2, \frac{1}{2}-2z_2$	0.41,	0.41,	0.46	4.2
$y_2-x_2, y_2-x_2, 2z_2$	0.34,	0.34,	0.04	3.8
$x_1+x_2, y_1+y_2, \frac{1}{2}+z_1-z_2$	0.48,	0.15,	0.24	6.5
$y_1+x_2, x_1+y_2, \frac{1}{2}-z_1-z_2$	0.49,	0.19,	0.20	9.5
$-y_1+y_2, -x_1+x_2, -z_1+z_2$	0.08,	0.23,	0.26	3.4
$x_2-y_1, x_1-y_2, z_2+z_1$	0.26,	0.11,	0.30	5.8
$\frac{1}{2}-x_1-y_2, \frac{1}{2}+y_1-x_2, \frac{1}{4}+z_2-z_1$	0.31,	0.24,	0.49	5.9
$\frac{1}{2}-y_2-y_1, \frac{1}{2}-x_2+x_1, \frac{1}{4}+z_2+z_1$	0.35,	0.27,	0.05	3.8
$\frac{1}{2}-x_2-x_1, \frac{1}{2}-y_2+y_1, \frac{1}{4}-z_2-z_1$	0.02,	0.42,	0.45	8.6
$\frac{1}{2}-x_2-y_1, \frac{1}{2}-y_2+x_1, \frac{1}{4}-z_2+z_1$	0.01,	0.39,	0.01	9.2

The $|F(hk\ell)|^2$ values were modified by a function $M(\underline{S}) = \left\{ \hat{f} \exp \sin^2\theta/\lambda^2 \right\}^{-2}$ and the values of $|F(hk\ell)|^2 M(\underline{S})$ were used as the coefficients in the Patterson synthesis. The two-dimensional Patterson projection down the b-axis, P(UW), was computed with three hundred and thirty five terms. This projection contained a great many peaks and clearly offered no hope of providing the bromine co-ordinates. Accordingly the three-dimensional Patterson map was computed with 1190 terms.

The peaks to be expected on the three Harker sections of the three-dimensional Patterson synthesis, $P(U,\frac{1}{2},W)$, $P(U,V,\frac{1}{4})$ and $P(U,V,\frac{1}{2})$ are, in themselves, insufficient to define fully the two sets of bromine co-ordinates. For example, the occurrence of a Br-Br vector at $2x,2y,\frac{1}{2}$ on $P(U,V,\frac{1}{2})$ does not distinguish the following x,y-co-ordinates, x,y; $\frac{1}{2}-x,y$; $x,\frac{1}{2}+y$; $\bar{x},y$. In a similar fashion the peaks on the section $P(U,\frac{1}{2},W)$ due to vectors at $\frac{1}{2}-2x,\frac{1}{2}.\frac{1}{4}-2z$, and $\frac{1}{2}-2y,\frac{1}{2},\frac{1}{4}+2z$ could be caused by bromine atoms having any of the sets of x and y co-ordinates listed above. The vectors on the section $P(U,V,\frac{1}{4})$ at $\frac{1}{2}-x+y$, $\frac{1}{2}-y-x$, $\frac{1}{4}$, however, enable a distinction to be drawn between on the one hand the co-ordinates (x,y) or $(\bar{x},y)$ and on the other $(\frac{1}{2}-x,y)$ or $(x,\frac{1}{2}+y)$.

Peaks in general positions, due to vectors between symmetrically related bromine atoms enable a further distinction in the x and y co-ordinates to be drawn if the z- co-ordinates of the bromine atoms can assume complete freedom over the following eight positions, z, $\bar{z}$, $\frac{1}{2}+z$, $\frac{1}{2}-z$, $\frac{1}{4}+z$, $\frac{1}{4}-z$, $\frac{3}{4}+z$, $\frac{3}{4}-z$. In this way, by inspection of the peaks due to symmetrically related heavy atoms, the x- and y- co-ordinates of the two bromine atoms can be found. Thereafter, any possible interchanges of the x- and y- co-ordinates and all possible positions of the z- co-ordinate have to be tested by studying the vector sets due to all possible non-equivalent combinations and superimposing them on the Patterson function to find which gives the best agreement. Difficulty may arise if the peaks in general positions due to vectors between heavy atoms related by symmetry cannot readily be picked out from those due to vectors between heavy atoms unrelated by symmetry.

The section of the three-dimensional Patterson synthesis $P(U,\frac{1}{2},W)$, Fig.I, should contain two peaks due to each set of symmetrically related bromine atoms. The peaks should be at $\frac{1}{2}-2x_1$, $\frac{1}{2}$, $\frac{1}{4}-2z_1$ and $\frac{1}{2}-2y_1$, $\frac{1}{2}$, $\frac{1}{4}+2z_1$ for $Br_1(x_1, y_1, z_1)$ and at $\frac{1}{2}-2x_2$, $\frac{1}{2}$, $\frac{1}{4}-2z_2$ and

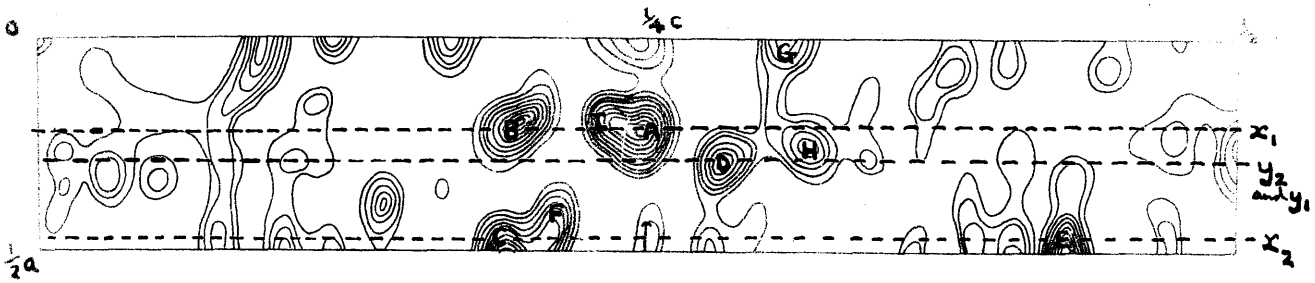


FIG. I.

The three-dimensional Patterson function, section P(U,½,W). The contours are drawn at arbitrary intervals. The peaks and lines referred to in text are marked on the tracing sheet.

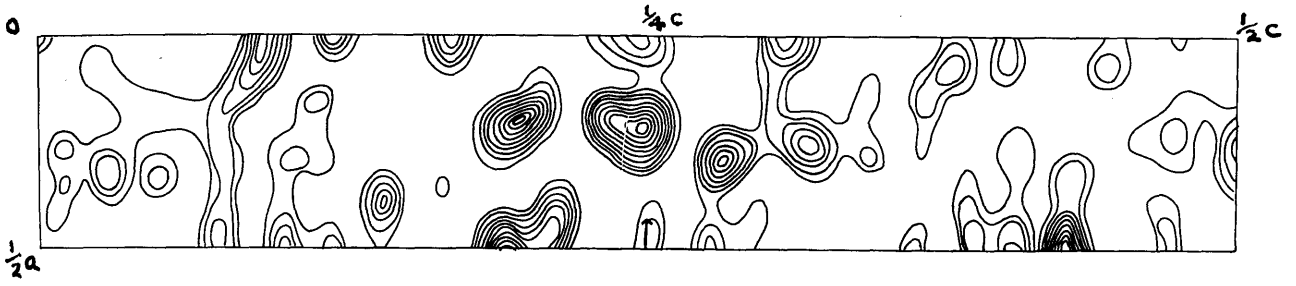


FIG. I.

The three-dimensional Patterson function, section P(U,½,W). The contours are drawn at arbitrary intervals. The peaks and lines referred to in text are marked on the tracing sheet.

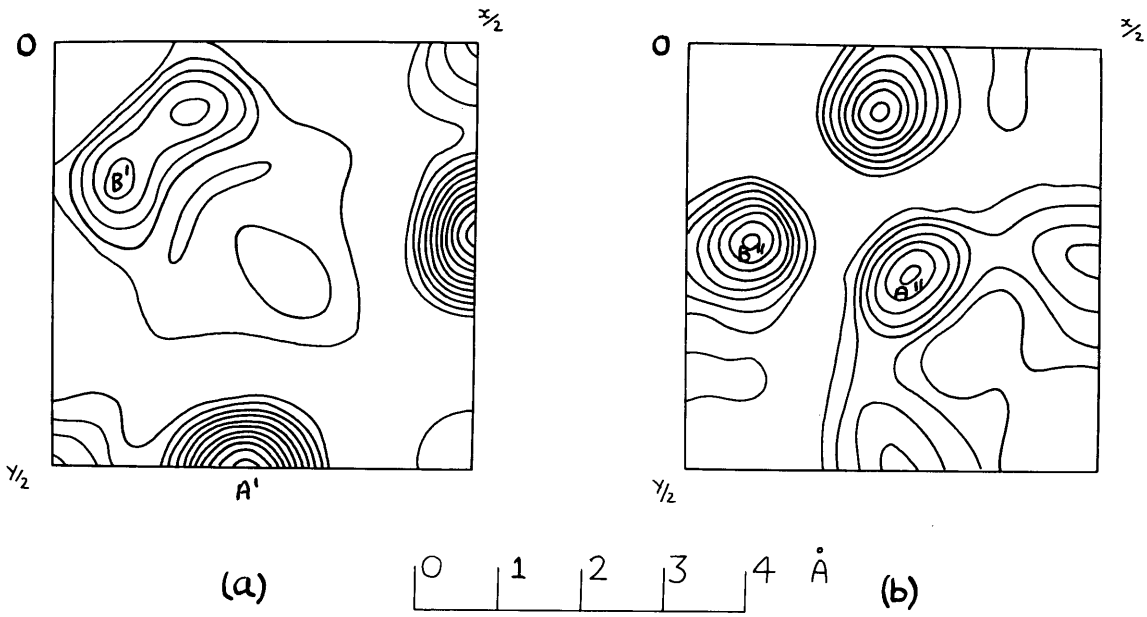


Fig.II. The three-dimensional Patterson function.
Sections: a) $P(U,V,\frac{1}{4})$
b) $P(U,V,\frac{1}{2})$
Contour levels are arbitrary. The peaks mentioned in text are shown.

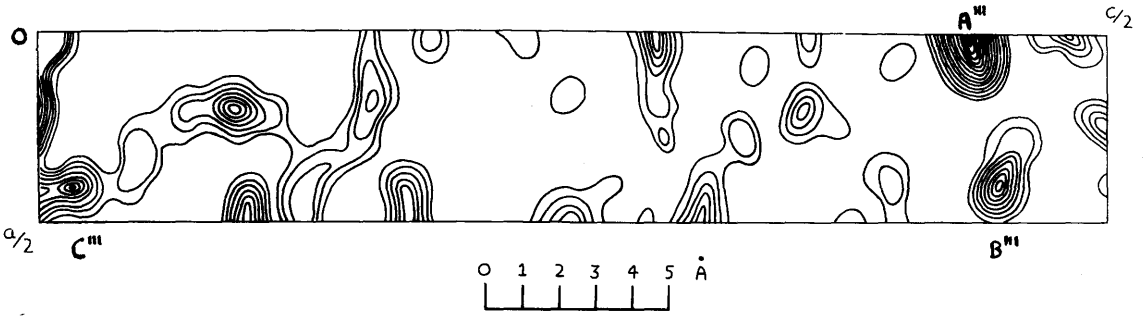


Fig. III. The three-dimensional Patterson function, section P(U,0,W). Contour levels are arbitrary, the levels at the origin have been omitted. The peaks mentioned in the text are marked on the photograph.

$\frac{1}{2}-2y_2$, $\frac{1}{2}$, $\frac{1}{4}+2z_2$ for $Br_2(x_2, y_2, z_2)$. The ideal vector set on this section would be two peaks for each heavy atom at an equal and opposite distance from the line $P(U,\frac{1}{2},\frac{1}{4})$.

The large peak (A) that occurs at $W/4$ is soon to be recognised as representing vectors lying on the section $P(U,V,\frac{1}{4})$, so its presence on the section $P(U,\frac{1}{2},W)$ probably has no special significance. It is not symmetrical about $W/4$ and there may be a genuine Harker peak at (I). In the region of the section, $W = 0 \rightarrow W/4$, the two largest peaks are (B) and (C), (B) is attenuated and may represent two vectors, while near (C) there is a smaller maximum at (F). In the region of the section $W = \frac{1}{4}$ to $\frac{1}{2}$, the largest peaks are (D) and (E), neither of which can correspond to either (B) or (C). While no peak can be found at an equal and opposite distance from $W/4$ as (E), the peaks (I) or (F) could represent the complement of (D). Similarly, (G) or (H) could correspond to either (B) or (C).

The Harker section $P(U,V,\frac{1}{4})$, Fig.II(a), should contain four peaks at $\frac{1}{2}-x_1 -y_1$, $\frac{1}{2}-x_1+y_1$; $\frac{1}{2}-x_2-y_2$, $\frac{1}{2}-x_2+y_2$; $\frac{1}{2}-x_1+y_1$, $\frac{1}{2}-x_1-y_1$; $\frac{1}{2}-x_2+y_2$, $\frac{1}{2}-x_2-y_2$; the first two being related to the last two by symmetry. The most obvious

choices are the peak (A'), i.e. the peak that occurs on $P(U,\frac{1}{2},W)$ and the peak (B'). These peaks correspond to about the same height, allowing for the fact that(A') is made up of two unresolved vectors related by a mirror plane; these two unresolved vectors need not be coincident with $U/2$. The forthcoming discussion will be simplified by assuming that (A') represents the vector $\frac{1}{2}-x_1-y_1$, $\frac{1}{2}-x_1+y_2$ and that (B') represents the vector $\frac{1}{2}-x_2-y_2$, $\frac{1}{2}-x_2+y_2$.

On the section $P(U,V,\frac{1}{2})$, Fig.II(b), there should be four peaks at $2x_1$, $2y_1$; $2x_2$, $2y_2$; $2y_1$, $2x_1$; $2y_2$, $2x$; the first two being related to the last two by symmetry. The peaks (A") and (B") were picked as being the most likely to represent these vectors. These two peaks can be made to correspond with the peaks (A') and (B') from the section $P(U,V,\frac{1}{4})$ if the y- co-ordinate obtained for Br_2 from peak (B") on the section $P(U,V,\frac{1}{2})$ is changed to $\frac{1}{2}-y$.

The selection of peaks from the sections $P(U,V,\frac{1}{4})$ and $P(U,V,\frac{1}{2})$ narrows the search for the Br-Br vectors on the section $P(U,\frac{1}{2},W)$ to those that lie on the lines drawn on Fig.I. The peaks (C), (F) and (E) all lie on the line for the vector $(\frac{1}{2}-2x_2,\frac{1}{2},\frac{1}{4}-2z_2)$ while on the

corresponding line for the vector ($\frac{1}{2}-2y_2$, $\frac{1}{2}$, $\frac{1}{2}+2z_2$) the peaks (H) and (D) could match (C) and (F) respectively. In the case of the other bromine atom, the peaks (B) and (I) could be matched with (H) or (D) respectively.

The emergence of several alternative heavy atom co-ordinates from a study of the three Harker sections, led to a search for peaks due to Br-Br vectors in general positions in the Patterson map. In particular, special attention was given to the section P(U,0,W) as the occurrence of a great many peaks on the section P(U,$\frac{1}{2}$,W) when only four are to be expected suggests that the values of some of the co-ordinates (x_1, y_1, x_2, y_2) must be very similar and consequently a concentration of vectors can be expected on P(U,0,W). This section is shown in Fig.III.

There are several large peaks on this section, but all those that represent vectors less than 4 Å can be safely neglected. There are three peaks (A'''), (B''') and (C''') which probably represent Br-Br vectors; of those (A''') is of particular interest as U = V suggesting that it represents one of the vectors between symmetrically related bromine atoms at ($x+y$, $x+y$, $\frac{1}{2}-2z$) or ($y-x$, $y-x$, $2z$). Taking (A''') as representing the vector ($y-x$, $y-x$, $2z$) for Br_1 and the peaks (B) and (H) as representing ($\frac{1}{2}-2x$, $\frac{1}{2}$, $\frac{1}{4}-2z$) and ($\frac{1}{2}-2y$, $\frac{1}{2}$, $\frac{1}{4}+2z$) respectively will give a consistent

set for x_1, y_1, z_1. Furthermore, as (H) is not a very high peak, it is unlikely to represent two vectors on the section P(U,$\frac{1}{2}$,W). On this assumption, the most likely peaks to represent the vectors $\frac{1}{2}-2x_2$, $\frac{1}{2}$ $\frac{1}{4}-2z_2$ and $\frac{1}{2}-2y_2$, $\frac{1}{2}$, $\frac{1}{4}+2z_2$ are (F) and (D) respectively. This solution of the Patterson gives the most probable basic set of co-ordinates for both bromine atoms (Table III). The heights and co-ordinates of the peaks to be expected from symmetry related bromine atoms are given in Table II.

From this basic set of co-ordinates, the actual co-ordinates were derived by considering the peaks due to interactions between bromine atoms, unrelated by symmetry. A process of trial and error was followed, considering all the possible non-equivalent sets of co-ordinates related by symmetry to the basic set. One set of such co-ordinates gave vectors that corresponded to higher values of the function P(UVW) than any of the others. The co-ordinates of these vector peaks are given in Table II, as are the values of the function P(UVW) corresponding to these peaks. The co-ordinates of the bromine atoms thus obtained are given in Table III.

Of the peaks occurring on the section P(U, $\frac{1}{2}$, W) other than true Harker peaks, the peak (I) and the

attenuation of (B) can be accounted for by vectors between non-symmetrically related bromine atoms, while on the section P(U,O,W), two of the heavier peaks (B''') and (C''') on Fig.(V) are due to vectors between non-symmetrically related atoms.

TABLE III

The Basic and Final Sets of Bromine Co-ordinates as fractions of the Unit Cell.

	x_1	y_1	z_1	x_2	y_2	z_2
Basic Set	0.150	0.113	0.223	0.038	0.338	0.017
Final Set	0.150	0.113	0.223	0.338	0.038	0.483

N.B. The numbering of these two atoms does not correspond to the chemical numbering given in the discussion, etc.

TABLE IV.

3-D Patterson Synthesis

↓ 2 Br atoms

S.F. I (B_θ = 4, R = 48%)

Fourier I (1027 terms)

↓ 16 C atoms + 2 Br atoms

S.F. II. (B_θ = 4, R = 39%)

Fourier II (1075 terms)

↓ 30 C atoms + 2 Br atoms

S.F. III (B_θ = 5, R = 31%)

Fourier III (1114 terms)

↓ 29 C, 4O, 4N + 2 Br atoms

S.F. IV (B_θ = 5.5, R = 26%)

Fourier IV (1184 terms)

↓ 29 C, 4 O, 4 N, 2 Br atoms

S.F. V (B_θ = 6, R = 22%)

Fourier V (all 1190 terms) $F_o + F_c$ syntheses.

↓ 30 C, 4 O, 4 N, 2 Br atoms

S.F. VI (B_θ = 6, R = 20%)

Fourier VI (all terms) $F_o + F_c$ synthesis

↓ all atoms

- Cont'd -

TABLE IV. (Cont'd)

S.F. VII (B_θ = 6.75 for Br, 6.42 other atoms; R = 19%)

Fourier VII (F_o + F_c syntheses)

↓ all atoms

S.F. VIII (Individual B values, R = 18.1%)

Least Squares Cycle I.

↓ $\Sigma w\Delta^2 = 2420$

Final Structure Factor Calculation

(Individual Isotropic B_θ values,

R = 16.8%)

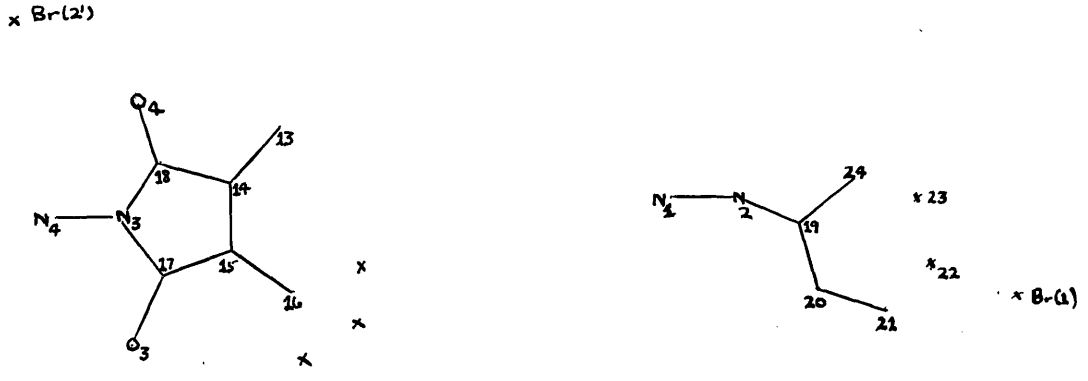
II. The Solution of the Structure.

The ratio $\frac{\sum f_H^2}{\sum f_L^2}$ for the p-bromophenylhydrazine derivative of byssochlamic acid is 1.568. This value indicates that the determination of phases by calculation on the basis of the bromine positions should be closer to the true phases than in the case of clerodin bromolactone.

Structure factors calculated from the positions of the bromine atoms showed a discrepancy between observed and calculated values of 48%. Some difficulty was encountered in attempting to calculate an electron density distribution on the basis of the heavy atom phases and observed structure amplitudes, as the DEUCE Fourier series program could not handle the Fourier expression for the space group $P4_12_12$ in the normal manner. The most convenient way of computing a Fourier series for this space group is to reduce the point group of the crystal from 422 to its sub-group 222. (This was done at the suggestion of Dr. T.A.Hamor.) It involves doubling the number of atoms in the asymmetric unit and including more than the basic non-equivalent set of $F_o(hk\ell)$ values. Under these conditions, and if the origin is changed to $(\frac{1}{4}, 0, \frac{3}{8})$, the space group becomes

effectively $P2_12_12_1$ with two molecules in the asymmetric unit; these molecules should prove identical if the multiplicities of the tetragonal system are preserved.

The first Fourier map was then computed with 1027 terms together with those generated by the multiplicities of the system. Several chemical features could be identified in it. A five-membered ring (IV) with a substituent on each atom seemed to indicate that the derivative formed with p-bromophenyl-hydrazine preserved the five-membered ring of the parent anhydride (II). By following the direction of the C(15) - C(16) bond, several other electron density maxima could be discerned in chemically aceptable sites.



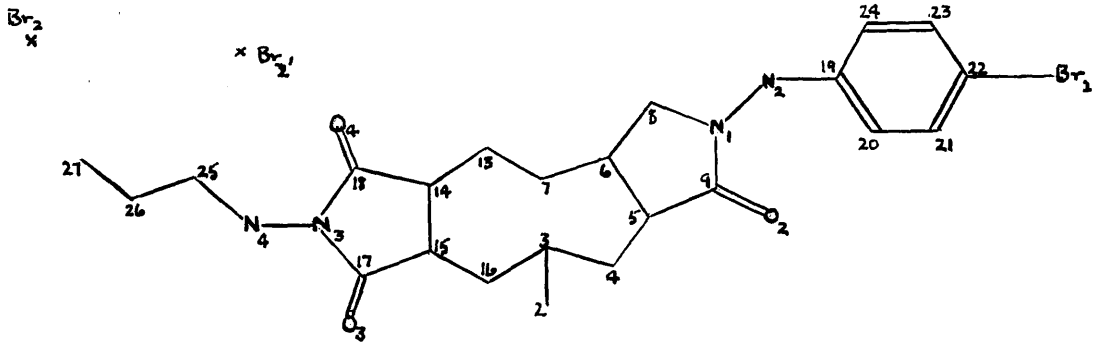
(IV)

The two atoms O(3) and O(4) did not appear to be attached to any other atoms, so it was assumed that they were

probably the oxygen atoms attached to the five-membered ring. It was evident that one of the bromine atoms, Br(1), was attached to a benzene ring which had a substituent in the para position, although two of the atoms, C(22) and C(23) in the six-membered ring were noticeably out of the plane of the ring. The point of attachment of the other bromine atom, Br(2'), could not be discerned. Although the complete structure was not apparent from this map, the amount of genuine detail shown in the map confirmed the choice of bromine co-ordinates and allowed sixteen atoms other than bromine to be selected for inclusion in the next structure factor calculation. These were the atoms C(13), C(14), C(15), C(16), C(17), C(18), C(19), C(20), C(21), C(24), N(1), N(2), N(3), N(4), O(3) and O(4).

The second structure factor calculation caused a drop in the discrepancy from 48% to 39%, and 1075 terms were used to compute a second Fourier synthesis. All the atoms included in the previous cycle came up to a satisfactory height. By following the chain of atom sites attached to C(15), a nine-membered ring could be seen re-joining the five-membered ring at C(14) (V). Furthermore, the outline of a second five-membered ring could be distinguished joining the nine-membered ring

at C(5) and C(6). This second five-membered ring contained N(1) and was attached to the planar and six-membered ring found in the first Fourier map by means of the nitrogen atom N(2). One of the supposed oxygen atoms attached to this five-membered ring was considerably out of the plane of the other atoms comprising the (-C—C(=O)—N) group at this stage in the phasing calculations, so it was not included in the next cycle of structure factor calculations. An atom, C(2), could be seen attached to C(3) and there were several other maxima in this region which might prove to represent genuine atoms, including some evidence for a four-membered ring. The two atoms



(V)

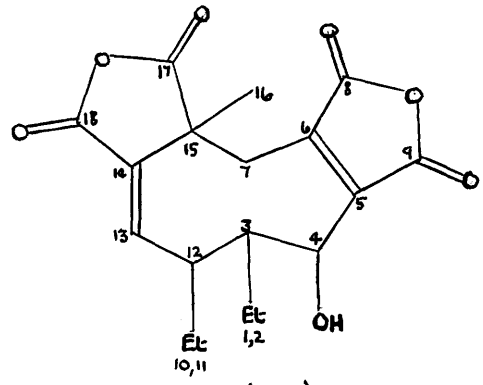
C(22) and C(23) of the planar six-membered ring omitted in the second structure factor calculation because they were out of the plane of the ring had moved to more

acceptable positions. It was also evident that the bromine atom, Br(2'), nearest to N(3) and N(4) was in fact too near them to be attached to them via a benzene ring bonded to N(4). However, a symmetrically related bromine atom, Br(2), could be seen at about the correct distance (5.6 - 6.0 Å) from N(4). The details of this six-membered ring remained rather indistinct, only three atoms being sufficiently clear to warrant inclusion in the phasing calculations. The partial structure obtained at this stage is shown in (V).

All thirty light atoms marked in (V) were included in the third cycle of structure factor calculations. This calculation gave a discrepancy between observed and calculated structure amplitudes of 31%. From the output of this calculation, a Fourier series was evaluated with 1114 terms.

In addition to the thirty light atoms other than hydrogen shown in (V), the positions of four of the remaining eight atoms are roughly known (i.e. there are three atoms in a benzene ring and the oxygen atom attached to C(8). From the formula of the derivative it can be shown that there should be seventeen double bond equivalents in the molecule, of which fifteen can be

accounted for. At this time, information came to hand about the structure of glauconic acid ($C_{18}H_{20}O_7$), on which Professor Barton had been working. This compound is related to the glaucanic acid isolated by Wijkman. The structure of glauconic acid is shown in (VI). (The stereochemistry was not at this time known.)

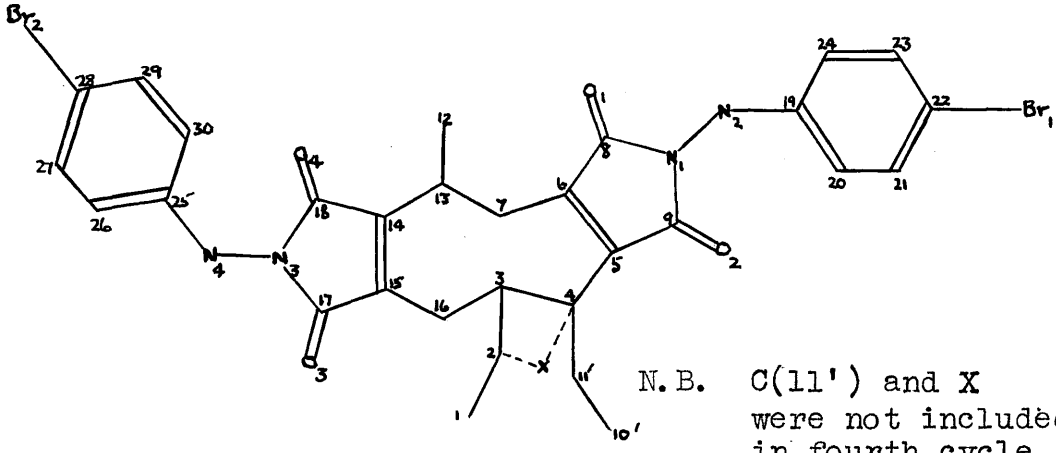


(VI)

In the present context, the two most interesting features of this structure are the double bonds in the nine-membered ring and the ethyl groups attached to the ring. This information proved helpful, in that the presence of two double bonds in the nine-membered ring of byssochlamic acid was soon established to account for the last two double bond equivalents; it also proved misleading in that a rather too conscious search for ethyl groups was undertaken.

In the third Fourier map (VII), the last three atoms of the benzene ring and the oxygen atom attached to C(8) were clearly distinguishable, but the remaining four atoms proved more difficult to locate. There was a peak

C(1) close to C(2) and together these atoms would form an ethyl group attached to C(3). The traces of a four-membered ring in this region of the molecule were less pronounced on this map. There was quite a high peak C(10') at a distance of about 2.3 Å from C(4) and this, coupled with a smaller maximum C(11') nearer C(4) suggested the possibility of an ethyl group attached to C(4) (c.f. glauconic acid). The values of the peak



N.B. C(11') and X were not included in fourth cycle.

(VII)

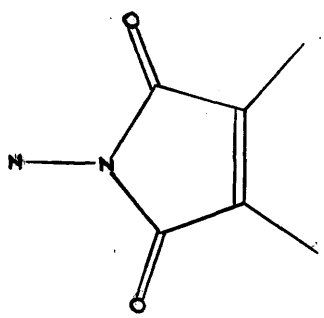
heights of these atoms in the second and third Fourier maps are listed in Table V.

TABLE V.
(Peak Heights in electrons/Å^3.)

	C(2)	C(1)	C(11')	C(10')	X
Fourier II	2.85	1.92	1.52	1.35	1.44
Fourier III	5.03	2.37	1.39	2.24	1.48

Another peak, C(12) could be seen attached to C(13) and came up to a height of 2.83 electrons/$\mathring{A}^3$, and a further 1.5 $\mathring{A}$ away from this peak there was another peak of 2.15 electrons/$\mathring{A}^3$ which might be a diffraction 'ripple' from one of the bromine atoms as it had similar y- and z- co-ordinates.

On the assumption that there are two double bonds in the nine-membered ring, models of the various possible structures were constructed. It was found that the only model that could simulate the real conformation of the ring was one with double bonds between C(5) and C(6), and C(14) and C(15). These locations for the double bonds were substantiated by the close planarity of the two parts of the molecule of the type shown in (VIII).



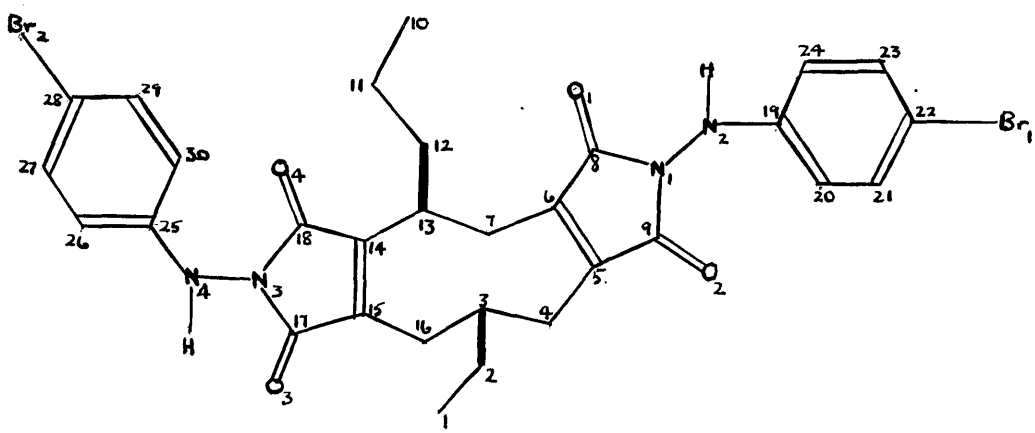
(VIII)

Atoms C(10'), C(12), C(1), C(28), C(29), C(30), and O(1) together with those included in the third structure factor calculation were used to calculate the phases for the next Fourier synthesis. By omitting C(11') and including C(10'), a decisive test of the correctness of placing an ethyl group

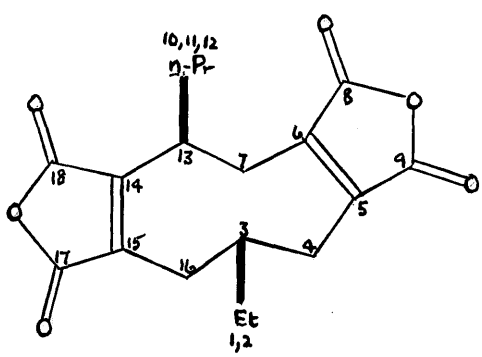
at C(4) could be made. The Fourier map so obtained provided clear evidence that there was no ethyl group attached to C(4). The peak C(10'), although included in the phasing calculations, only came up to a height of 2.1 electrons/$\mathring{A}^3$ compared to over 4.0 electrons/$\mathring{A}^3$ for the majority of the other carbon atoms. This indicates that the peak is a spurious effect due to inaccurate phasing. The peak C(11') came up to a height of 1.48 electrons/$\mathring{A}^3$ whereas the peak C(11) near C(12) came up to a height of 2.61 electrons/$\mathring{A}^3$. The two atoms C(11) and C(12) would, therefore, appear to form an ethyl group attached to C(13). The possibility of C(11') being a genuine methyl group was tested by calculating over one hundred structure factors on the basis of the other thirty seven light atoms together with the two bromine atoms (a) with C(11') included, and (b) without C(11'). The latter calculation gave a significantly lower R- factor and it was therefore considered that C(11') was a false peak.

A further cycle of structure factor and Fourier calculation was carried out, Fourier syntheses being evaluated with both $|F_o|$ and $|F_c|$ as coefficients with the calculated phases. An atom, C(10) was located

attached to C(11), with a height of 2.35 electrons/$\mathring{A}^3$ in the F_o map and less than 1 electron/$\mathring{A}^3$ in the F_c map. This atom forms a n-propyl group with C(11) and C(12) attached to C(13). The structure and relative stereochemistry of byssochlamic acid bis-p-bromophenyl-hydrazide and of byssochlamic acid itself are illustrated in (IX) and (X) respectively.



(IX)



(X)

Refinement:

The R- factor for the fifth cycle of structure factor calculations was 22%. On inclusion of the last atom, C(10), and new co-ordinates for the other atoms in the phasing calculations, the R- factor fell to 20%. Two cycles of structure factor calculations and Fourier syntheses, using both $|F_o|$ and $|F_c|$, as Fourier coefficients and employing 'back-shift' corrections to the positions of the atoms in the F_o map reduced the R- factor to 18.1%. Isotropic temperature factors (B_θ) were assigned to each atom individually from a comparison of the peak heights in both F_o and F_c syntheses for inclusion in the seventh and eighth structure factor calculations. It was found that the temperature factors for the two bromine atoms were the highest ($B_\theta = 7.10$), whereas the average value for the carbon atoms in the ring system was much lower, while the atoms C(1), C(2), C(10), C(11), and C(12) showed intermediate values.

At this stage, it was realised that further Fourier refinement would be relatively ineffective. The structure and relative stereochemistry had been determined and much further refinement was thought unnecessary. The bond lengths calculated from the

co-ordinates worked out from the seventh Fourier series made chemical sense.

It was decided to carry out one cycle of least squares refinement on the data to see if this resulted in any significant shifts in atomic positions. No attempt was made to locate hydrogen atom positions or to include hydrogen atoms in the calculations at any stage. The cycle of least squares was undertaken with the following weighting scheme,

$$\sqrt{w(hk\ell)} = \frac{|F_o(hk\ell)|}{43.0} \quad \text{if} |F_o| < 43.0$$

$$\sqrt{w(hk\ell)} = \frac{43.0}{|F_o(hk\ell)|} \quad \text{if} |F_o| \geqslant 43.0$$

The new sets of co-ordinates did not show many changes from those included in the calculation and the thermal parameters, b_{ij}, obtained from the least squares treatment did not indicate any marked anisotropic thermal motion. Accordingly, the equivalent isotropic temperature factors (B_θ) for the atoms were used with the new co-ordinates to calculate the final set of structure factors which had a discrepancy of 16.8%, without considering unobserved reflexions. The listed values of HKL , $|F_o|$, $|F_c|$, and α are given in Table VI. The unobserved reflexions are

included in this table with their maximum possible observed value. The final isotropic temperature factors are listed in Table VII.

The form factors used for carbon, oxygen, and nitrogen atoms were those of Berghuis et al. (1955), and that for bromine was the Thomas-Fermi curve (Internationale Tabellen, 1935).

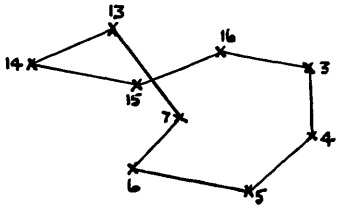
TABLE VII.

Final Isotropic Temperature Factors.

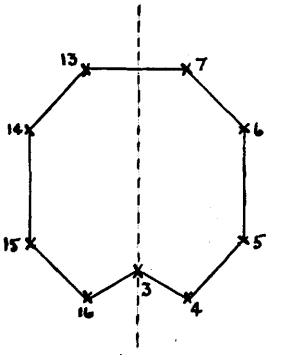
	B_{θ}		B_{θ}
C(1)	6.4	C(21)	5.6
C(2)	6.4	C(22)	5.6
C(3)	4.7	C(23)	5.6
C(4)	4.7	C(24)	5.6
C(5)	5.0	C(25)	5.6
C(6)	4.7	C(26)	5.6
C(7)	4.7	C(27)	5.6
C(8)	5.0	C(28)	5.6
C(9)	4.7	C(29)	5.6
C(10)	6.4	C(30)	5.6
C(11)	6.4	O(1)	5.6
C(12)	6.4	O(2)	5.6
C(13)	4.7	O(3)	5.6
C(14)	5.0	O(4)	5.6
C(15)	4.7	N(1)	5.6
C(16)	4.7	N(2)	5.6
C(17)	4.3	N(3)	5.6
C(18)	4.3	N(4)	5.6
C(19)	5.6	Br(1)	6.8
C(20)	5.6	Br(2)	6.8

Results and Conclusions:

The final three-dimensional electron density map of byssochlamic acid bis-p-bromophenylhydrazide is shown in Fig. IV as superimposed contour sections drawn parallel to (1,0,0) and covering the region of one molecule. The corresponding atomic arrangement is shown in Fig.V. It can be seen that the conformation adopted by the nine-membered ring is a type of 'boat' (XI). This ring is formed by two groups of four atoms held in a plane inclined to each other at an angle of about 25°, with a ninth atom, C(3), acting



(XI)



(XII)

as a 'hinge'. This atom could take up several positions along a plane of symmetry through the ring (XII). This is not an exact plane of symmetry as the ring is in an

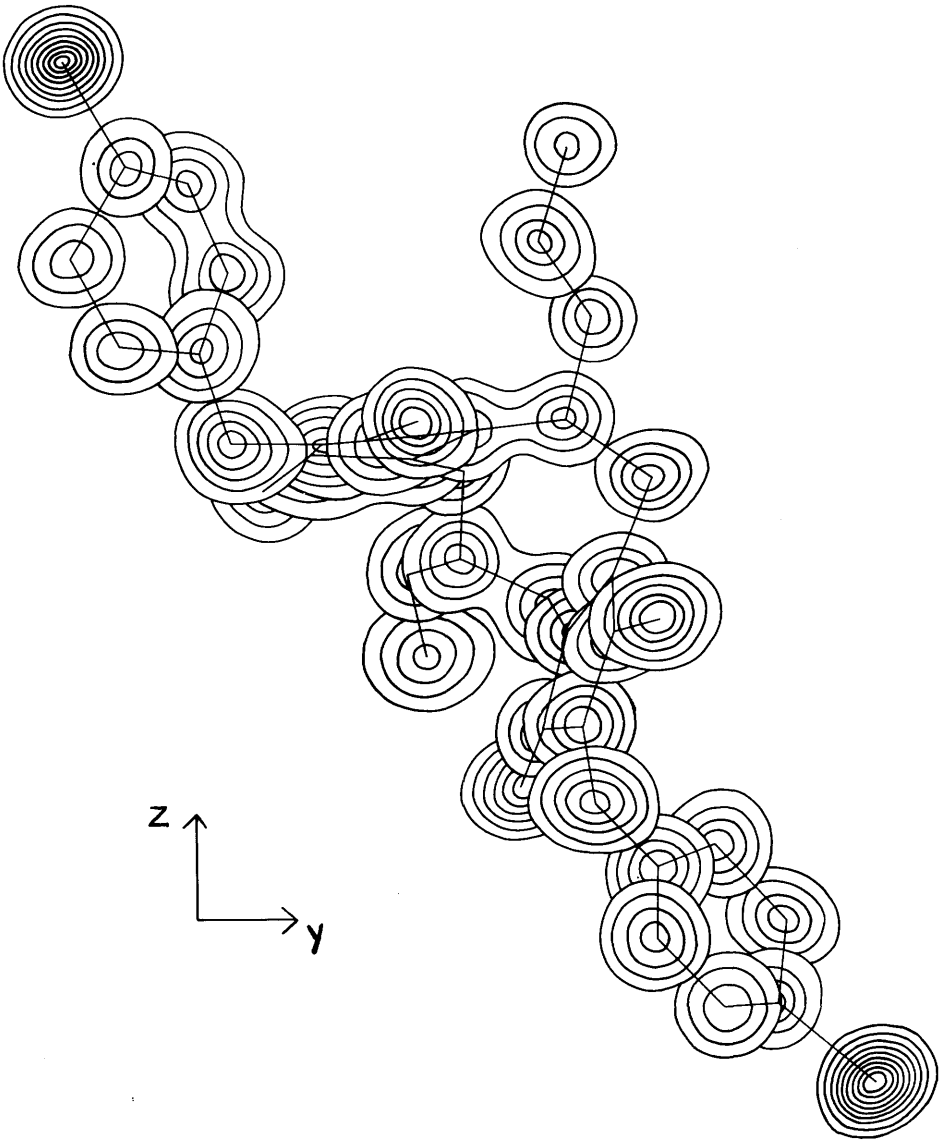


Fig.IV. The final three-dimensional Fourier map, drawn as superimposed contour section parallel to (100). Contour interval is 1 electron/Å^3, the lowest contour being 2 electrons/Å^3. For the bromine atoms, the interval is 3 electrons/Å^3.

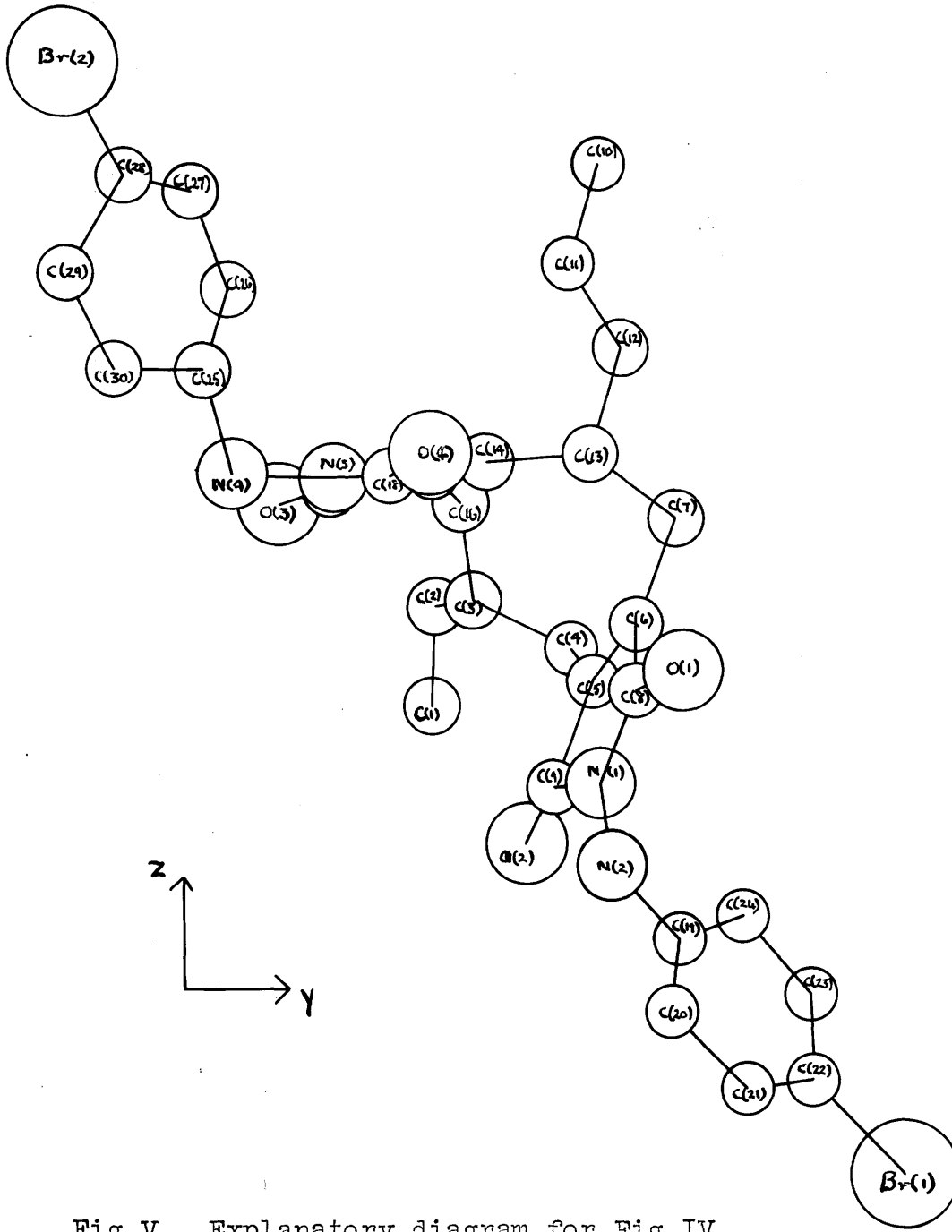


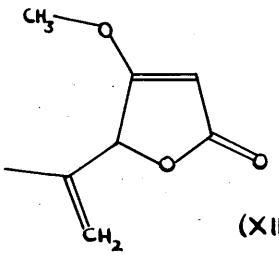
Fig.V. Explanatory diagram for Fig.IV. The atom numbers are marked, except C(15) and C(17) which are hidden.

unsymmetrical environment, but it serves as a useful illustration. The intramolecular non-bonded distances across the ring are given in Table XIII. The ethyl and n-propyl groups are attached to the nine-membered ring in positions CIS to each other.

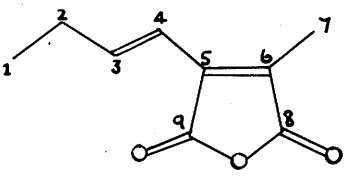
The biosynthesis of byssochlamic acid and the related glauconic and glaucanic acids has been discussed by Baldwin, Barton, Bloomer, Jackman, Rodriguez-Hahn, and Sutherland (1962). The schemes of biogenesis envisaged are illustrated in Table VIII.

Bentley and Keil (1961) have shown that another fungal metabolite, penicillic acid (XIII), can be derived from acetate and malonate units. Preliminary work by Barton and his colleagues has shown that glaucanic acid (XV), glauconic acid (XVI), and byssochlamic acid (XVII) can be derived from acetate units. They have also shown that glauconic acid can be derived from two units having identical carbon skeleton (XIV). The oxidation level of glauconic and glaucanic acids is such that if one of these dienoid units formed an anion, the whole carbon skeleton of glaucanic acid could be formed with the ethylenic linkages in the correct positions. Accepting this

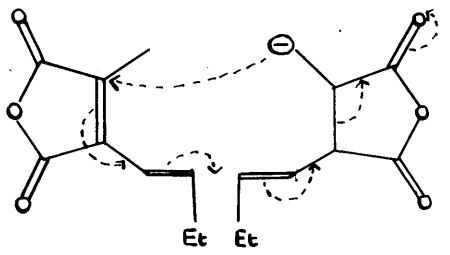
TABLE VIII.

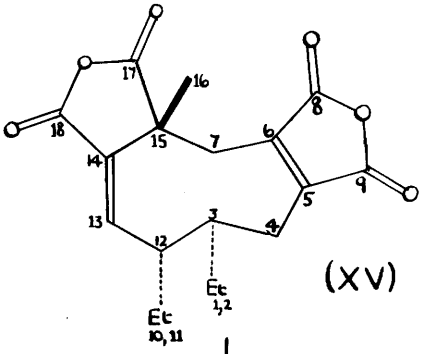


(XIII)

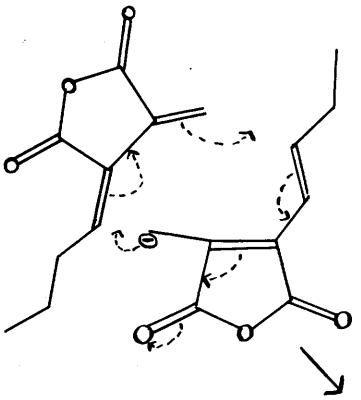


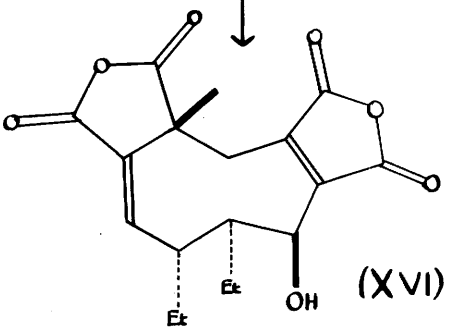
(XIV)



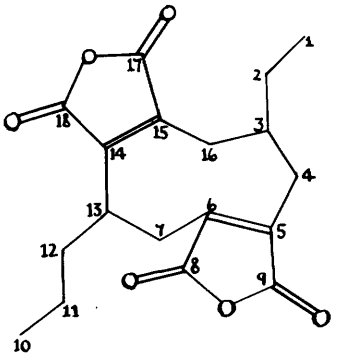


(XV)





(XVI)



(XVII)

hypothesis, the hydroxyl group of glauconic acid could be introduced at a later stage in the biogenesis by biochemical hydroxylation of glaucanic acid. Barton has shown that the carbon skeleton of this dienoid unit is derivable from an intermediate citric acid. Byssochlamic acid can be formed from the same biogenetic units by a similar type of mechanism.

Ferguson and Sim (1962) have elucidated the structure of the m-iodobenzoate of glauconic acid and they find the stereochemistry to be that shown in the Table. This differs from that proposed by Barton in the stereochemical attachment of the hydroxyl group at C(4), but this will not affect Barton's theory of biogenesis.

The final atomic co-ordinates, relating to one molecule, obtained from the least squares output are given in Table IX. The standard deviations in the positional parameters of the atoms, calculated from the least squares output are given in Table X. The interatomic bond lengths, together with the standard deviations are given in Table XI, while the interbond angles are listed in Table XII. The average standard deviation in bond angles is 4.5°. The important

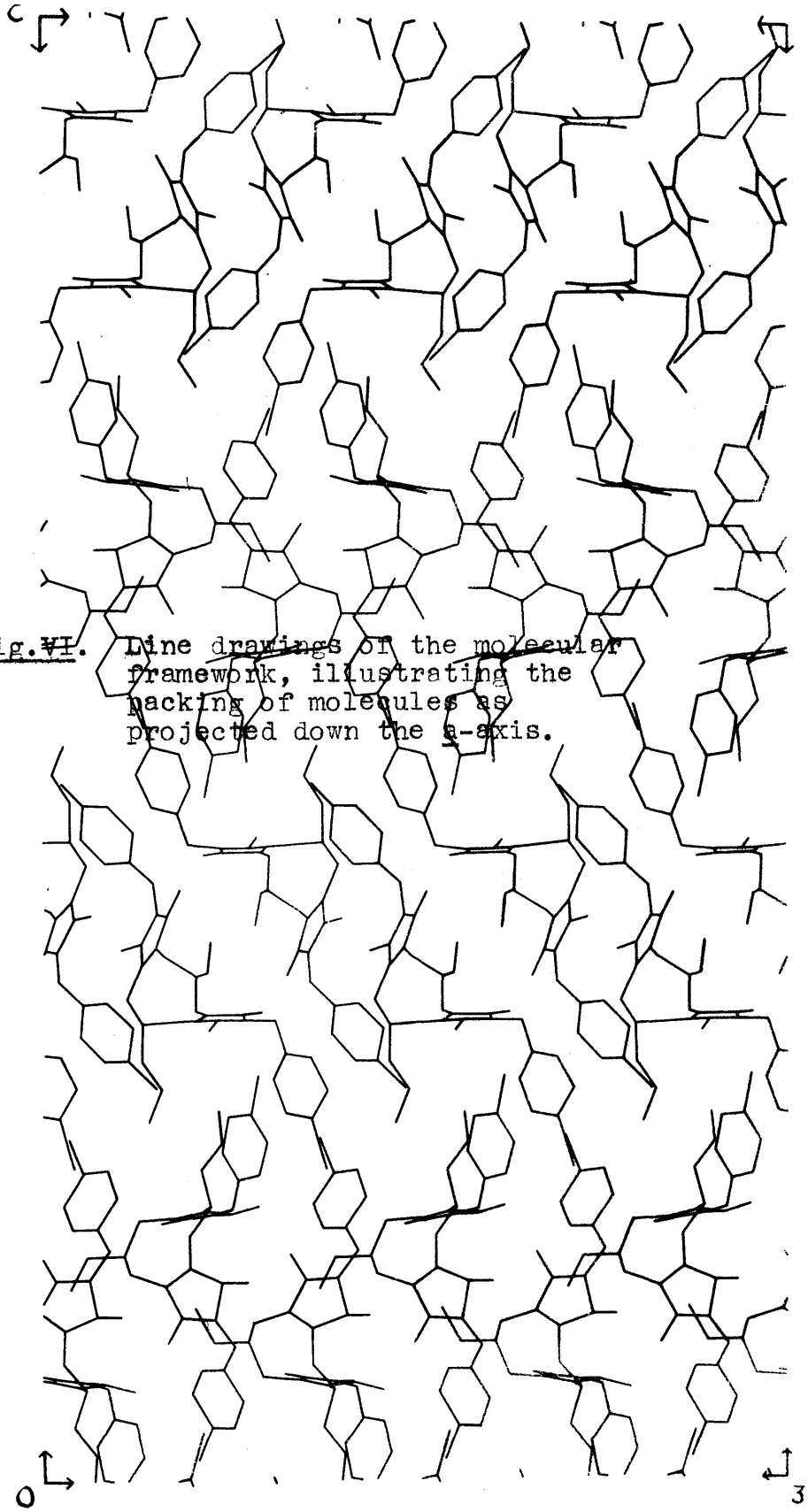
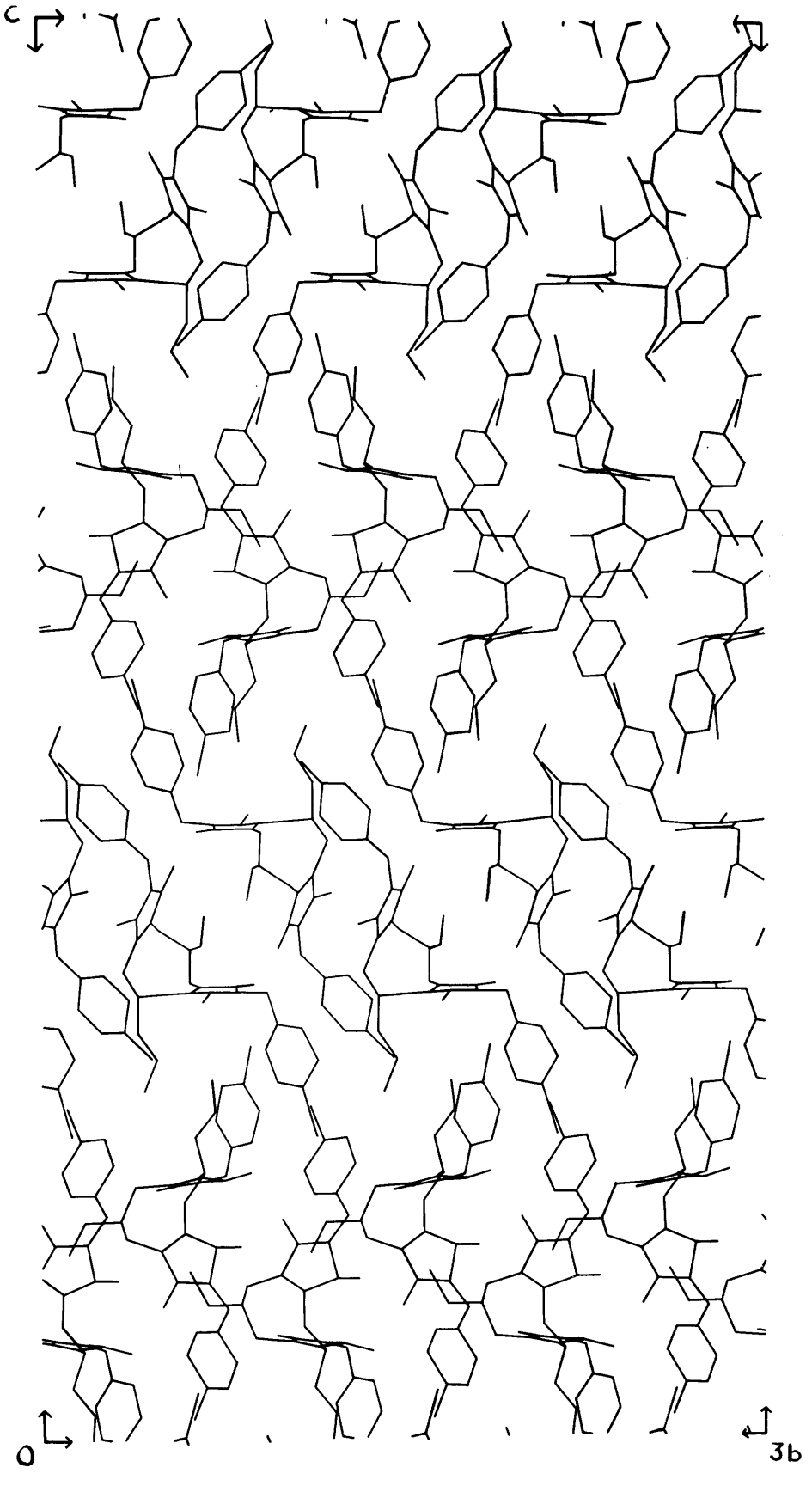


Fig.VI. Line drawings of the molecular framework, illustrating the packing of molecules as projected down the a-axis.

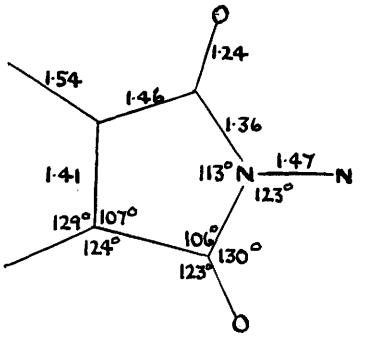

c
0
3b

non-bonded distances within the molecule are given in Table XIII, while all intermolecular distances less than 4 Å are listed in Table XIV.

The packing of molecules viewed down the a- axis is illustrated in Fig.VI.

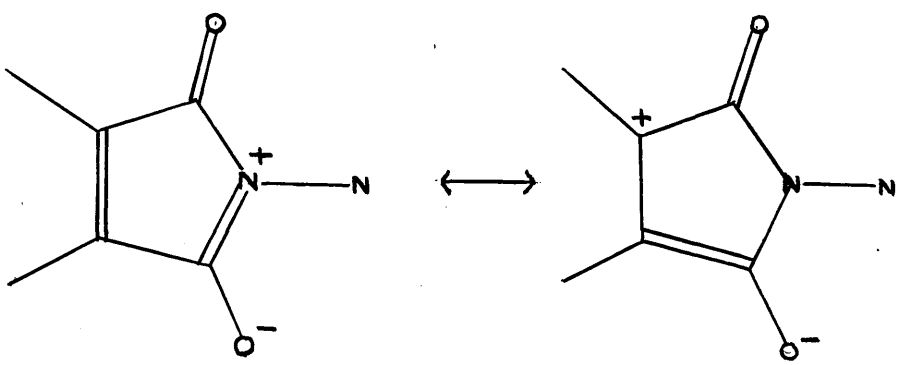
With standard deviations in bond length of the order of 0.08 Å, it is unwise to draw meaningful conclusions about molecular dimensions. This unfavourable situation is somewhat ameliorated in the bromo-anilino imide grouping where at least two estimates of similar bond lengths and angles can be made.

The average bond length in the aromatic rings is 1.39 Å and the average single bond between two tetrahedral carbon atoms is 1.53 Å ; in both cases the agreement with accepted values is satisfactory. The dimensions of the five-membered rings are interesting and the average values are shown in (XVIII). It is assumed when taking these averages, that environmental factors are similar in all cases.



(XVIII)

The angles suggest that the nitrogen atom in the ring is tending towards sp^2 hybr idisation. From the valence-bond standpoint, this would indicate that resonance structures of the type shown in (XIX)(a) are important



(a) (b)

(XIX)

Trueblood, Goldish, and Donohue (1961) estimate that a σ- bond between trigonal nitrogen and trigonal carbon is 1.41 Å, hence the value of 1.36 Å found here suggests significant double bond character. A similar shortening of the carbon-nitrogen bond is found in succinimide (Mason, 1961) and in N-chlorosuccinimide (Brown, 1961) and a shortening of the carbon-oxygen bond in the five-membered ring of maleic anhydride is found by Marsh, Ubell, and Wilcox (1962). Taking the C(sp^2)single bond radius to be 0.735 Å (Trueblood, Goldish and Donohue, 1961, and Craig and Mason, unpublished results reported by Mason, 1961), the expected value for a single

bond between trigonally hybridised carbon atoms would be 1.47 Å, i.e. the value found in maleic anhydride, and very near to that found in the present work. The conclusion that there is relatively little double bond character in this carbon-carbon bond is supported by the results of Darlow and Cochran (1961) and Darlow (1961) for the maleate ion. This conclusion, however, is not supported by the carbon-carbon length of 1.41 Å found for the bond fusing the five-membered ring to the nine-membered ring. If the resonance structure (XIX(b)) had no importance, this bond would have a length of about 1.33 Å. The length of this bond in (XVIII) is, however,only the average of two values, whereas all the other bonds discussed are the average of four values.

The best plane that could be fitted to the atoms of the five-membered rings and the atoms bonded to them was found by a least squares treatment (Schomaker et al.,1959). The equation for the plane C(14) - C(18) is $0.005\ X' - 0.003\ Y' + 0.999\ Z' + 25.01 = 0$. The deviations from this plane are large, but the χ^2 significance test indicates that the accuracy of the analysis is insufficient to prove aplanarity. The equation for the plane C(5) - C(9) is $0.139\ X' + 0.392\ Y' - 0.909\ Z' - 7.41 = 0$, where a similar situation pertains. In the succinimide, N-chlorosuccinimide, and maleic anhydride structures

a small, but significant degree of aplanarity is found. The sums of the internal angles of the two five-membered rings add up to 538.6° and 540.1° respectively. The sum of the internal angles of a planar five-membered ring should be 540°, although this is not, of course, a sufficient condition to prove planarity.

The angles of the five-membered rings are much less than tetrahedral on account of strain. The C-N-C angle is also greater than the other angles, a point found in the succinimide and N-chlorosuccinimide structures, but not in maleic anhydride in the case of the C-O-C angle. This possibly indicates a greater tendency towards sp^3 hybridisation for the oxygen atom in maleic anhydride than the nitrogen atoms have in the present work and in succinimide.

In carboxylic acids and acid amides, where X = O or N respectively, the X - C = O and C - C = O angles are substantially greater than the X - C - C angle (Table XV). This effect is due to repulsion by the lone pairs of electrons on the oxygen which is double bonded to carbon. This situation is found to an even greater extent in compounds where the atom X participates in a five-membered ring. In carboxylic acids and acid amides, the differences in the X - C = O and C - C = O

angles are slight, yet in maleic anhydride, succinimide, N-chlorosuccinimide, and isatin (Goldschmidt and Llewellyn, 1950), the C - C = O angle is very much greater than the X - C = O angle, a fact that Marsh, Ubell, and Wilcox attribute to double bond character in the C - C bond in maleic anhydride. In the present analysis, the situation is reversed with the X - C = O angle found to be 130° and the C - C = O to be 123°. This effect could perhaps be due to strain brought about by the N-p-bromo-anilino group, although this is not found in the case of the chlorine atom in N-chloro-succinimide. The distances between the oxygen atoms of the five-membered rings and the atoms of the N-p-bromo-anilino group are not shorter than normal (Table XIII). The thesis of Marsh and collaborators is difficult to accept in view of the results found for succinimide.

The initial assumption that environmental factors can be ignored may be invalid as several short non-bonded distances involving oxygen atoms are listed in Table XIV. In particular, O(2) and O(3) are involved in close contacts of 2.94 Å and 2.86 Å respectively with nitrogen atoms, probably involving hydrogen bonds. The closest carbon-oxygen non-bonded distance is 3.27 Å, and the closest contact between carbon atoms of neighbouring

molecules is 3.44 Å. The benzene rings adopt a very close-packed condition, as can be seen by the large number of short distances between atoms in rings of neighbouring molecules.

The very large values found for C(24)C(19)N(2) and C(26)C(25)N(4) angles can partially be explained due to overcrowding between C(24) and N(1) and between C(26) and N(3). These non-bonded interactions are 2.97 Å and 2.76 Å respectively, which is considerably less than would be expected under normal conditions. The effect cannot be very great, however, as the benzene rings in the individual molecule would have considerable freedom of motion, by rotation around either the C - N or N - N bonds. Such rotations do occur, but not to any great extent, as can be shown from the distances given in Table XIII. If a great deal of rotation about these bonds did take place, not only would it affect the forces on the atoms of the five-membered rings, but it would also make it more difficult for the derivative to crystallise with such a close packed structure.

Such rotations as do occur about the N - N and C - N bonds effectively place the atoms of the five-membered rings in an unsymmetrical environment, and may partially account for some of the unusual dimensions found therein.

TABLE IX.

Atomic Co-ordinates.

	x/a	y/b	z/c
C(1)	0.3966	-0.1639	0.37981
C(2)	0.3299	-0.1444	0.40382
C(3)	0.1836	-0.1048	0.40285
C(4)	0.1689	0.0208	0.39092
C(5)	0.0220	0.0498	0.38355
C(6)	-0.0842	0.1134	0.39670
C(7)	-0.0686	0.1669	0.42254
C(8)	-0.2037	0.1158	0.38282
C(9)	-0.0458	0.0146	0.36242
C(10)	-0.1862	0.0801	0.50436
C(11)	-0.1998	0.0425	0.48182
C(12)	-0.1234	0.1065	0.46089
C(13)	-0.1559	0.0569	0.43791
C(14)	-0.1362	-0.0838	0.43558
C(15)	-0.0193	-0.1456	0.43063
C(16)	0.1285	-0.1030	0.42948
C(17)	-0.0452	-0.2928	0.43096
C(18)	-0.2441	-0.1805	0.43427
C(19)	-0.2048	0.1569	0.32657
C(20)	-0.2851	0.1491	0.30626

- Cont'd -

TABLE IX. - Cont'd -

Atomic Co-ordinates.

	x/a	y/b	z/c
C(21)	-0.2681	0.2407	0.28790
C(22)	-0.1551	0.3307	0.28969
C(23)	-0.0870	0.3518	0.31011
C(24)	-0.1238	0.2617	0.32717
C(25)	-0.2664	-0.4664	0.45792
C(26)	-0.2075	-0.4227	0.47588
C(27)	-0.2268	-0.4681	0.49899
C(28)	-0.3192	-0.5643	0.50242
C(29)	-0.3736	-0.6510	0.48358
C(30)	-0.3528	-0.5723	0.45996
O(1)	-0.3009	0.1754	0.38605
O(2)	0.0173	-0.0433	0.34538
O(3)	0.0579	-0.3792	0.42822
O(4)	-0.3504	-0.1554	0.43917
N(1)	-0.1707	0.0541	0.36296
N(2)	-0.2568	0.0612	0.34170
N(3)	-0.1831	-0.3018	0.43314
N(4)	-0.2518	-0.4256	0.43539
Br(1)	-0.1131	0.4561	0.26649
Br(2)	-0.3574	-0.6279	0.53119

TABLE X.

Standard Deviations

in Atomic Position (in Å).

	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$
C(1)	0.065	0.064	0.051
C(2)	0.064	0.069	0.053
C(3)	0.056	0.059	0.045
C(4)	0.059	0.056	0.047
C(5)	0.055	0.065	0.049
C(6)	0.053	0.059	0.044
C(7)	0.057	0.055	0.045
C(8)	0.057	0.063	0.047
C(9)	0.065	0.053	0.044
C(10)	0.064	0.069	0.052
C(11)	0.067	0.070	0.056
C(12)	0.066	0.064	0.050
C(13)	0.058	0.061	0.047
C(14)	0.062	0.058	0.047
C(15)	0.056	0.062	0.048
C(16)	0.061	0.057	0.044
C(17)	0.062	0.057	0.045
C(18)	0.060	0.058	0.048
C(19)	0.063	0.066	0.049

- Cont'd -

TABLE X. - Cont'd -

Standard Deviations

in Atomic Position (in Å).

	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$
C(20)	0.063	0.066	0.051
C(21)	0.063	0.062	0.051
C(22)	0.061	0.059	0.053
C(23)	0.061	0.062	0.050
C(24)	0.067	0.061	0.047
C(25)	0.063	0.067	0.049
C(26)	0.062	0.064	0.048
C(27)	0.063	0.064	0.053
C(28)	0.059	0.066	0.049
C(29)	0.063	0.062	0.047
C(30)	0.061	0.059	0.049
O(1)	0.039	0.042	0.033
O(2)	0.039	0.043	0.034
O(3)	0.040	0.045	0.030
O(4)	0.040	0.039	0.033
N(1)	0.046	0.056	0.041
N(2)	0.051	0.053	0.040
N(3)	0.050	0.050	0.044
N(4)	0.051	0.052	0.041
Br(1)	0.009	0.009	0.026
Br(2)	0.008	0.008	0.023

TABLE XI.

Interatomic Bond Lengths in Å,
with estimated Standard Deviations

C(1) - C(2)	1.550 ± 0.086	C(17) - N(3)	1.397 ± 0.075
C(2) - C(3)	1.527 ± 0.081	C(18) - O(4)	1.136 ± 0.066
C(3) - C(4)	1.448 ± 0.075	C(18) - N(3)	1.368 ± 0.073
C(3) - C(16)	1.632 ± 0.075	C(19) - N(2)	1.402 ± 0.076
C(4) - C(5)	1.566 ± 0.075	C(19) - C(20)	1.425 ± 0.084
C(5) - C(6)	1.458 ± 0.074	C(19) - C(24)	1.534 ± 0.082
C(5) - C(9)	1.440 ± 0.075	C(20) - C(21)	1.414 ± 0.084
C(6) — C(7)	1.592 ± 0.074	C(21) - C(22)	1.458 ± 0.082
C(6) - C(8)	1.445 ± 0.076	C(22) - C(23)	1.378 ± 0.081
C(7) - C(13)	1.668 ± 0.077	C(22) - Br(1)	1.887 ± 0.060
C(8) - O(1)	1.163 ± 0.067	C(23) - C(24)	1.388 ± 0.082
C(8) - N(1)	1.344 ± 0.074	C(25) - N(4)	1.369 ± 0.077
C(9) - O(2)	1.307 ± 0.066	C(25) - C(26)	1.271 ± 0.084
C(9) - N(1)	1.319 ± 0.071	C(25) - C(30)	1.381 ± 0.084
C(10) - C(11)	1.360 ± 0.089	C(26) - C(27)	1.421 ± 0.084
C(11) - C(12)	1.569 ± 0.088	C(27) - C(28)	1.357 ± 0.084
C(12) - C(13)	1.452 ± 0.082	C(28) - C(29)	1.389 ± 0.082
C(13) - C(14)	1.437 ± 0.078	C(28) - Br(2)	1.818 ± 0.060
C(14) - C(15)	1.362 ± 0.078	C(29) - C(30)	1.498 ± 0.082
C(14) - C(18)	1.460 ± 0.078	N(1) - N(2)	1.503 ± 0.068
C(15) - C(16)	1.550 ± 0.077	N(3) - N(4)	1.432 ± 0.068
C(15) - C(17)	1.505 ± 0.078		
C(17) - O(3)	1.364 ± 0.067		

TABLE XII.

Interbond Angles.

C(1)	- C(2)	- C(3)	115°	C(13)	- C(14)	- C(15)	126°
C(2)	- C(3)	- C(4)	110°	C(13)	- C(14)	- C(18)	124°
C(2)	- C(3)	- C(16)	107°	C(15)	- C(14)	- C(18)	109°
C(4)	- C(3)	- C(16)	114°	C(14)	- C(15)	- C(16)	135°
C(3)	- C(4)	- C(5)	113°	C(14)	- C(15)	- C(17)	107°
C(4)	- C(5)	- C(6)	129°	C(16)	- C(15)	- C(17)	116°
C(4)	- C(5)	- C(9)	129°	C(3)	- C(16)	- C(15)	111°
C(6)	- C(5)	- C(9)	101°	C(15)	- C(17)	- O(3)	120°
C(5)	- C(6)	- C(7)	124°	C(15)	- C(17)	- N(3)	104°
C(5)	- C(6)	- C(8)	109°	O(3)	- C(17)	- N(3)	136°
C(7)	- C(6)	- C(8)	126°	C(14)	- C(18)	- O(4)	123°
C(6)	- C(7)	- C(13)	103°	C(14)	- C(18)	- N(3)	105°
C(6)	- C(8)	- O(1)	128°	O(4)	- C(18)	- N(3)	129°
C(6)	- C(8)	- N(1)	105°	C(20)	- C(19)	- C(24)	114°
O(1)	- C(8)	- N(1)	126°	C(20)	- C(19)	- N(2)	105°
C(5)	- C(9)	- O(2)	121°	C(24)	- C(19)	- N(2)	139°
C(5)	- C(9)	- N(1)	111°	C(19)	- C(20)	- C(21)	121°
O(2)	- C(9)	- N(1)	128°	C(20)	- C(21)	- C(22)	117°
C(10)	- C(11)	- C(12)	125°	C(21)	- C(22)	- C(23)	123°
C(11)	- C(12)	- C(13)	117°	C(21)	- C(22)	- Br(1)	123°
C(12)	- C(13)	- C(7)	98°	C(23)	- C(22)	- Br(1)	113°
C(12)	- C(13)	- C(14)	113°	C(22)	- C(23)	- C(24)	112°
C(7)	- C(13)	- C(14)	105°	C(19)	- C(24)	- C(23)	132°

- Cont'd -

TABLE XII - Cont'd -

Interbond Angles.

C(26) - C(25) - C(30) 119°	C(25) - C(30) - C(29) 118°
C(26) - C(25) - N(4) 128°	C(8) - N(1) - C(9) 113°
C(30) - C(25) - N(4) 112°	C(8) - N(1) - N(2) 122°
C(25) - C(26) - C(27) 126°	C(9) - N(1) - N(2) 123°
C(26) - C(27) - C(28) 117°	C(19) - N(2) - N(1) 109°
C(27) - C(28) - C(29) 120°	C(17) - N(3) - C(18) 113°
C(27) - C(28) - Br(2) 122°	C(17) - N(3) - N(4) 123°
C(29) - C(28) - Br(2) 117°	C(18) - N(3) — N(4) 124°
C(28) - C(29) - C(30) 118°	C(25) - N(4) - N(3) 114°

TABLE XIII.

Intramolecular Non-bonded Distances.(in Å).

C(1) ... C(4)	3.02	C(7) .... C(15)	3.22
C(3) ... C(6)	3.50	C(7) ... C(16)	3.39
C(3) ... C(7)	3.90	C(7) ... C(18)	3.98
C(3) ... C(13)	4.29	C(7) ... O(1)	3.15
C(3) ... C(14)	3.74	C(8) ... C(13)	3.26
C(3) ... C(17)	3.39	C(8) ... C(14)	3.71
C(3) ... O(3)	3.37	C(8) ... C(19)	3.27
C(4) ... C(7)	3.35	C(8) ... C(24)	3.62
C(4) ... C(13)	4.26	C(9) ... C(19)	2.98
C(4) ... C(14)	4.14	C(9) ... C(24)	3.31
C(4) ... C(15)	3.41	C(11) ... O(4)	3.51
C(4) ... O(2)	3.10	C(13) ... C(16)	3.32
C(5) ... C(13)	3.61	C(13) ... O(1)	3.53
C(5) ... C(14)	3.65	C(13) ... O(4)	2.90
C(5) ... C(15)	3.38	C(16) ... O(3)	2.87
C(5) ... C(16)	3.24	C(17) ... C(25)	3.23
C(6) ... C(14)	3.04	C(17) ... C(26)	3.33
C(6) ... C(15)	3.33	C(18) ... C(25)	3.19
C(6) ... C(16)	3.59	C(18) ... C(26)	3.44
C(7) ... C(11)	3.87	C(19) ... O(1)	3.57

- Cont'd -

TABLE XIII. - Cont'd -

Intramolecular

Non-bonded Distances (in Å).

C(19)	... O(2)	3.20
C(20)	... N(1)	3.59
C(24)	... O(1)	3.93
C(24)	... O(2)	3.54
C(24)	... N(1)	2.97
C(25)	... O(3)	3.79
C(25)	... O(4)	3.42
C(26)	... O(3)	3.86
C(26)	... O(4)	3.71
C(26)	... N(3)	2.76
C(30)	... N(3)	3.57
O(1)	... N(2)	2.84
O(2)	... N(2)	2.96
O(3)	... N(4)	3.18
O(4)	... N(4)	2.91

TABLE XIV.

Intermolecular Bond Lengths.
(< 4 Å)

The subscripts refer to the following equivalent positions:

I.	$x+1, y, z$	VI.	$y+1, x, \bar{z}$
II.	$x, y+1, z$	VII.	$\frac{1}{2}+y, \frac{1}{2}-x, \frac{3}{4}+z$
III.	$\frac{1}{2}+x, \frac{1}{2}-y, \frac{3}{4}-z$	VIII.	$\frac{1}{2}-y, \frac{1}{2}+x, \frac{1}{4}+z$
IV.	$\frac{1}{2}+x, -\frac{1}{2}-y, \frac{3}{4}-z$	IX.	$-\frac{1}{2}+x, \frac{1}{2}-y, \frac{3}{4}-z$
V.	$y, x, \bar{z}$		

O(3) ....N(2)^{IV}	2.86	O(2) ....C(30)^{IV}	3.64
O(2) ....N(4)^{IV}	2.94	C(2) ....O(2)^{IV}	3.67
Br(1)....C(27)^{VII}	3.25	C(10)....C(29)^{II}	3.67
O(3) ....C(20)^{IV}	3.27	O(3) ....C(19)^{IV}	3.69
C(4) ....O(1)^{III}	3.44	C(2) ....C(23)^{III}	3.70
C(27)....C(27)^{V}	3.44	C(22)....C(29)^{IV}	3.72
C(5) ....O(1)^{III}	3.48	C(27)....C(28)^{V}	3.72
C(1) ....O(2)^{IV}	3.49	C(1) ....N(3)^{IV}	3.73
C(28)....C(28)^{V}	3.50	C(11)....C(29)^{II}	3.73
C(4) ....C(24)^{III}	3.54	C(1) ....O(3)^{IV}	3.74
C(30)....Br(2)^{V}	3.55	C(10)....Br(2)^{II}	3.74
C(1) ....C(17)^{IV}	3.58	C(28)....C(29)^{V}	3.77
C(26)....C(27)^{V}	3.59	O(2) ....C(25)^{IV}	3.77
C(1) ....C(9)^{IV}	3.61	O(2) ....N(3)^{IV}	3.77
C(7) ....C(20)^{III}	3.62	Br(1)....C(28)^{VII}	3.78
C(20)....Br(2)^{IX}	3.64	C(2) ....O(4)^{I}	3.81

- Cont'd -

TABLE XIV. (Cont'd)

Intermolecular Bond Lengths.
(< 4 Å)

C(10)....C(28)^{II}	3.82	C(16)....C(10)^{V}	3.93
C(27)....N(4)^{V}	3.82	C(16)....C(22)^{III}	3.93
C(23)....C(30)^{IV}	3.85	C(24)....O(1)^{III}	3.93
C(25)....Br(2)^{V}	3.85	C(26)....C(28)^{V}	3.94
C(29)....Br(2)^{V}	3.86	O(3) ....Br(2)^{VI}	3.94
O(4) ....Br(2)^{V}	3.86	Br(1)....C(26)^{VII}	3.94
C(16)....C(23)^{III}	3.87	C(4) ....C(19)^{III}	3.96
O(2) ....O(4)^{IV}	3.87	C(4) ....C(23)^{III}	3.96
C(12)....C(29)^{II}	3.88	C(24)....C(30)^{IV}	3.96
C(23)....O(4)^{III}	3.88	C(28)....C(30)^{V}	3.97
C(7) ....C(21)^{III}	3.90	C(9) ....O(1)^{III}	3.98
C(12)....C(21)^{III}	3.90	C(12)....C(30)^{II}	3.98
C(15)....C(10)^{V}	3.90	C(27)....C(11)^{V}	3.98
C(10)....Br(1)^{VIII}	3.92	C(23)....C(29)^{IV}	3.99
C(26)....C(10)^{V}	3.92		

TABLE XV.

Comparison of dimensions
of Certain Acids and Amides.

Structure	C-C-X (°)	C-C=O (°)	O=C-X (°)	C-C (Å)	C-X (Å)	Ref. No.
Benzoic Acid	118	122	122	1.48	1.29	1
Benzamide	116	122	122	1.48	1.31	2
Acetic Acid	116	122	122	1.54	1.29	3
Acetamide	109	129	122	1.51	1.38	4
Oxalic Acid Dihydrate	113	122	126	1.53	1.29	5
Oxamide	115	120	126	1.54	1.32	6
Sorbic Acid	115	122	123	1.45	1.32	7
Crotonic Acid	113	122	125	1.50	1.30	7
Maleic Acid *	124	119	111	1.47	1.28	8
Maleate ion *	120	117	123	1.49	1.29	9
Maleic Anhydride	108	131	121	1.47	1.38	10
Succinimide	108	129	124	1.51	1.39	11
N-chlorosuccinimide	107	130	124	1.48	1.39	12

* Maleic Acid and Maleate ion both have six-membered rings due to hydrogen-bonding.

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PART III.

The Structure of Atrovenetin:

X-ray Analysis of a Trimethyl ether Ferrichloride of Atrovenetin.

The Structure of Atrovenetin:

X-ray Analysis of a Trimethyl ether Ferrichloride of Atrovenetin.

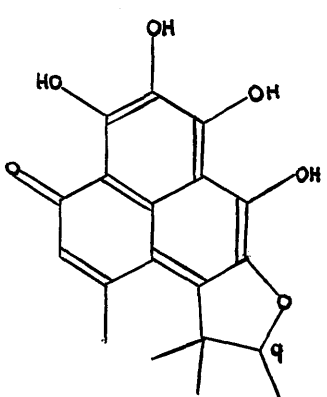
Introduction:

Atrovenetin ($C_{19}H_{18}O_6$) was isolated from *Penicillium atrovenetum* G. Smith by Neill and Raistrick (1957). The closely related species *P. Herquei* Bainier and Sartory has been shown (Stodola et al. 1951, Galarraga et al. 1955, and Harman et al., 1955) to contain herqueinone ($C_{19}H_{17}O_6$) and norherqueinone ($C_{19}H_{18}O_7$). Barton, de Mayo, Morrison, Schaeppi, and Raistrick (1956) showed that atrovenetin was identical with deoxynorherqueinone. Barton, de Mayo, Morrison, and Raistrick (1959) produced evidence for the structure (I), or its equivalent tautomer, to be that of atrovenetin. Later biogenetic and chemical evidence suggested that this structure might be incorrect, particularly in the point and manner of attachment of the five-membered ether ring.

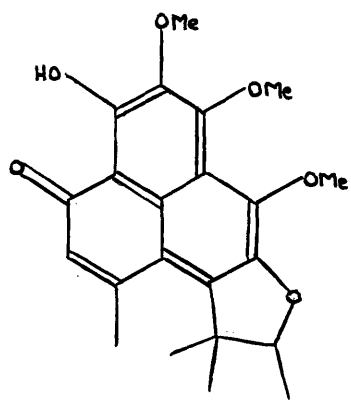
Neill and Raistrick (1957) prepared a large number of methyl ethers of atrovenetin, of which two were trimethyl ethers, one being orange, and the other yellow. Barton, de Mayo, Morrison, and Raistrick (1959) were able to show that assuming (I) to be the structure of atrovenetin,

the structures of the 'orange' and 'yellow' trimethyl ethers were (II) and (III) respectively. Barton was able to prepare crystalline derivatives of both trimethyl ethers by reacting them with ferric chloride in acid solution to form the ferrichloride salts. The derivative of the 'orange' trimethyl ether crystallised as thin red plates, while that of the 'yellow' trimethyl ether formed very thin orange lathes.

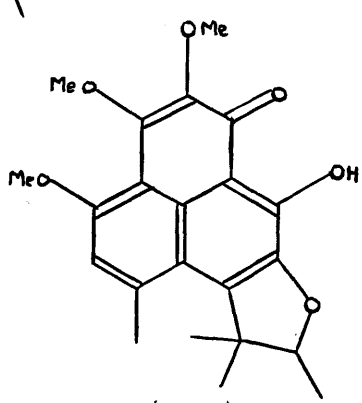
Preliminary photographs on both derivatives indicated that the ferrichloride salt of the 'orange' trimethyl ether would provide the more suitable material for X-ray analysis.



(I)



(II)



(III)

Experimental:

Atrovenetin Trimethyl Ether Ferrichloride ($C_{22}H_{24}O_6\ H^+, FeCl_4^-$) M = 582.8, m.p. 151-152°C., $d_{calc.}$ = 1.510 gm./cc., $d_{meas.}$ = 1.526 gm./cc. Monoclinic, a = 17.04 Å, b = 9.69 Å, c = 15.66 Å, β = 96°.35'; V = 2569 Å^3; no. of molecules/unit cell (Z) = 4; Absent Spectra, 0k0 when k is odd. Space Group $P2_1$ (C_2^2). Absorption coefficient for X-rays (λ = 1.542 Å) μ = 91 cm.$^{-1}$ F(000) = 1196.

The crystals of the atrovenetin derivative were in the form of very fine plates. The cell dimensions were obtained from precession photographs, and zero-layer and equi-inclination Weissenberg photographs were employed to collect the intensities by rotating the crystal about the symmetry axis. The intensities were estimated visually, the usual corrections being made, and then converted to structure amplitudes. In spite of the high linear absorption coefficient, no absorption corrections were thought necessary due to the very small cross-section of the crystals in the plane of the X-ray beam. The various zones were scaled according to exposure time, and at a later stage in the analysis, scaled relative to the calculated structure amplitudes. In all, 2,380 structure amplitudes were obtained.

Structure Determination:

(A) Determination of Heavy Atom Positions.

In the $h0\ell$ zone, the rows of reflexions where h is odd are either absent or very weak. As this effect is limited to the $h0\ell$ zone, it appears there must be a pseudo glide plane in the direction of the a- axis. As the atrovenetin molecule possesses an asymmetric centre at C(9), it could not crystallise in a space group containing a glide plane. The assumption was made that the pseudo glide plane probably only involves the heavy atom grouping, or indeed possibly just the iron atoms. This assumption is substantiated by the relatively weak structure amplitudes found in the rows where h is odd.

Accordingly, if the co-ordinates of the iron atom are x_1, y_1, z_1, those of the pseudo-related iron atom will be x_2, y_2, z_2 where,

$$x_2 = \tfrac{1}{2} + x_1 \quad \text{and} \quad z_2 = z_1$$

The vectors to be expected in the Patterson function are given in Table I.

TABLE I.

Equivalent Positions	x_1, y_1, z_1	$\frac{1}{2}+x_1, y_2, z_1$	$\bar{x}_1, \frac{1}{2}+y_1, \bar{z}_1$	$\frac{1}{2}-x_1, \frac{1}{2}+y_2, \bar{z}_1$
x_1, y_1, z_1	-	$\frac{1}{2}, y_1-y_2, 0$	$2x_1, \frac{1}{2}, 2z_1$	$\frac{1}{2}+2x_1, \frac{1}{2}+y_1-y_2, 2z_1$
$\frac{1}{2}+x_1, y_2, z_1$	$\frac{1}{2}, y_2-y_1, 0$	-	$\frac{1}{2}+2x_1, \frac{1}{2}+y_2-y_1, 2z_1$	$2x_1, \frac{1}{2}, 2z_1$
$\bar{x}_1, \frac{1}{2}+y_1, \bar{z}_1$	$-2x_1, \frac{1}{2}, -2z_1$	$\frac{1}{2}-2x_1, \frac{1}{2}+y_1-y_2, -2z_1$	-	$\frac{1}{2}, y_1-y_2, 0$
$\frac{1}{2}-x_1, \frac{1}{2}+y_2, \bar{z}_1$	$\frac{1}{2}-2x_1, \frac{1}{2}+y_2-y_1, -2z_1$	$-2x_1, \frac{1}{2}, -2z_1$	$\frac{1}{2}, y_2-y_1, 0$	-

The vectors so obtained would correspond to the set for the space group $P2_1/a$ if $y_2 = \frac{1}{2}-y_1$.

The Patterson function for the monoclinic system is:

$$P(UVW) = {}^{4}/_{V_c} \sum_{o}^{\infty}\sum_{o}^{\infty}\sum_{o}^{\infty} \left[\left(|F_o(hk\ell)|^2 + |F_o(hk\bar{\ell})|^2 \right) \cos 2\pi hU \cos 2\pi kV \cos 2\pi \ell W - \left(|F_o(hk\ell)|^2 - |F_o(hk\bar{\ell})|^2 \right) \sin 2\pi hU \cos 2\pi kV \sin 2\pi \ell W \right]$$

The Patterson projection P(UW) was computed with 248 terms, the coefficients of which were modified by a 'sharpening' function of the type described earlier. This projection is shown in Fig.I. The pattern is repeated to a first approximation in the interval ${}^{a}/_{2}$, with a pseudo origin at $({}^{a}/_{2},0)$. It was hoped that this projection would give information which would enable the disposition of the chlorine atoms around the iron atom to be elucidated. Quite apart from the question of pseudo-symmetry and possible different relative orientation in space of the chlorine atoms of the two molecules in the asymmetric unit, the possibility exists of the chlorine atoms being grouped either tetrahedrally, the more likely structure, or being disposed at the corners of a square.

Unfortunately, the highest non-origin peak (A) in the projection proved not to be the vector between

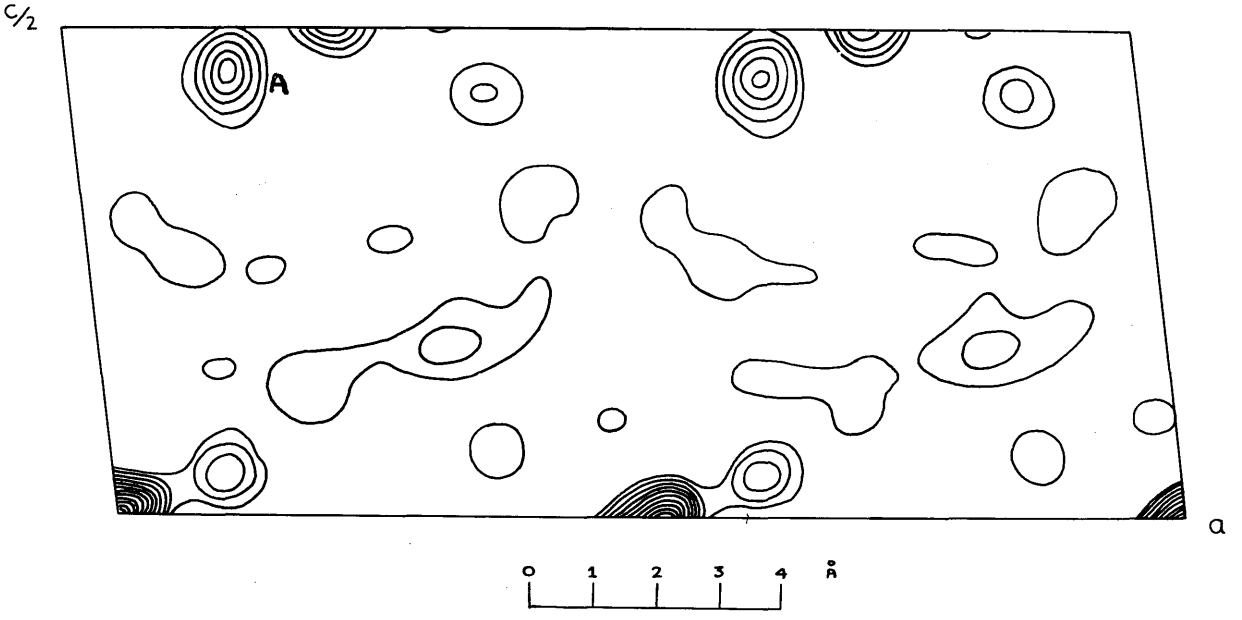


Fig.I. Two-dimensional Patterson projection down the b-axis, P(U,W). The contours are drawn on an arbitrary scale. The peaks referred to in the text are marked on the diagram.

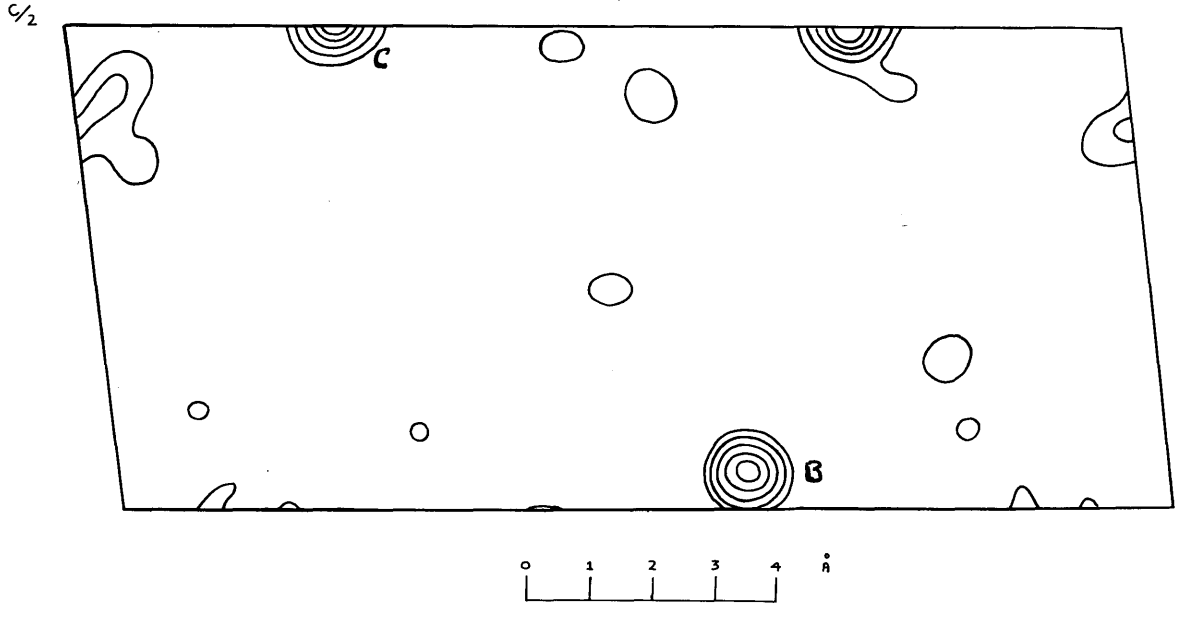


Fig.II. The three-dimensional Patterson function, section P(U,$\frac{1}{2}$,W). The contours are drawn on an arbitrary scale. The peaks referred to in text are marked on the diagram.

symmetrically-related iron atoms. As the two-dimensional approach had proved unhelpful, recourse was had to three-dimensional methods.

The three-dimensional Patterson map was computed with 2,380 terms. The section $P(U,\frac{1}{2},W)$ is shown in Fig.II. This section contains the vector $2x_1,\frac{1}{2},2z_1$ due to the iron atoms; it can be seen that there are two large peaks, (B) and (C), neither of which corresponds to the peak chosen from the P(UW) projection. There should be a peak on the line $P(\frac{1}{2},V,0)$ due to the vector at $\frac{1}{2},y_2-y_1,0$. A large maximum was found on this line at $V = {}^{9}/_{24}$, which thus corresponds to the difference in the y- co-ordinates of the iron atoms. Accordingly, there should be a peak corresponding to the vector $\frac{1}{2}+2x_1$, $\frac{1}{2}+y_1-y_2$, $2z_1$ on the section of the map, $P(U,{}^{3}/_{24},W)$. Examination of this section revealed peaks corresponding to the U- and W- values of both the large peaks on the section $P(U, \frac{1}{2}, W)$. The peak corresponding to the peak (B) on the section $P(U, \frac{1}{2}, W)$ lies very near to the origin and could not represent an Fe - Fe vector, but almost certainly represents either a Cl - Cl vector or an Fe - Cl vector. In this case, the peak (C) in Fig.II was taken as representing the vector at $(2x, \frac{1}{2}, 2z)$ due to the iron atoms. By choosing the origin on the b- axis

at a point mid-way between the y- co-ordinates of the two iron atoms, the following sets of co-ordinates for the iron atoms were obtained (Table II).

TABLE II.

	x/a	y/b	z/c
Fe(1)	0.126	0.321	0.249
Fe(2)	0.626	-0.321	0.249

The ratio of the square of the atomic number for iron to that of the sum of the squares of the other atoms is 0.286, which suggests that a calculation based on the position of the iron atom alone would not provide a reasonable approximation to the true phases and the interpretation of a Fourier map calculated with observed structure amplitudes and these phases might prove very difficult. An alternative procedure would be to attempt to locate the Fe - Cl vectors in the three-dimensional Patterson map and hence find the co-ordinates of the chlorine atoms. The ratio of the sum of the squares of the atomic numbers of known atoms to those of unknown atoms would then be 1.525, a much more favourable situation.

Superposition of the origin of the three-dimensional Patterson map on the iron positions revealed that there were four chlorine atoms grouped tetrahedrally around each iron atom, in positions exactly related by a glide plane along the a- axis. Thus, the deviation from the space group $P2_1/a$ must involve only the organic part of the structure. A structure factor calculation based on the position of the iron atom, and Fourier (F_o) sections at the expected positions of the chlorine atoms confirmed this conclusion and provided more accurate co-ordinates for the chlorine atoms. The discrepancy between observed and calculated structure amplitudes in this calculation was 73%. (This figure included the h0ℓ terms with h odd, which calculated zero.)

The expression for the structure factor for the space group $P2_1$ is given by:

$$A(hk\ell) = 2 \sum_{j}^{N/2} f_j \cos 2\pi(hx_j + \ell z_j) \cos 2\pi k y_j$$

$$B(hk\ell) = 2 \sum_{j}^{N/2} f_j \cos 2\pi(hx_j + \ell z_j) \sin 2\pi k y_j$$

when k is even

and,

$$A(hk\ell) = -2 \sum_{j}^{N/2} f_j \sin 2\pi(hx_j + \ell z_j) \sin 2\pi k y_j$$

$$B(hk\ell) = 2 \sum_{j}^{N/2} f_j \sin 2\pi(hx_j + \ell z_j) \cos 2\pi k y_j$$

when k is odd.

The expression for the electron density $\rho(XYZ)$ is

$$\rho(XYZ) = {}^{4}/_{V_c}\Bigg[\sum_{-\infty}^{\infty}\sum_{-\infty}^{\infty}\sum_{-\infty}^{\infty}\Big\{|A(hk\ell)|(\cos 2\pi hX \cos 2\pi kY \cos 2\pi\ell Z - \sin 2\pi hX \cos 2\pi kY \sin 2\pi\ell Z) + |B(hk\ell)|(\cos 2\pi hX \sin 2\pi kY \cos 2\pi\ell Z - \sin 2\pi hX \sin 2\pi kY \sin 2\pi\ell Z)\Big\}^{k=2n}$$

$$+ \sum_{-\infty}^{\infty}\sum_{-\infty}^{\infty}\sum_{-\infty}^{\infty}\Big\{|A(hk\ell)|(\cos 2\pi hX \sin 2\pi kY \sin 2\pi\ell Z - \sin 2\pi hX \sin 2\pi kY \cos 2\pi\ell Z) + |B(hk\ell)|(\sin 2\pi hX \cos 2\pi kY \cos 2\pi\ell Z - \cos 2\pi hX \cos 2\pi kY \sin 2\pi\ell Z)\Big\}^{k=2n+1}\Bigg]$$

(B) Scattering Curve for Iron.

The form factor for iron calculated by Freeman and Wood (1959) was accepted as the best available. Most calculations of atomic scattering factors assume that the frequency of the incident radiation (ω_i) is large in comparison to any absorption frequency (ω_k) of the scattering atom. This assumption is not valid in the case of iron scattering copper radiation. The K absorption edge for iron occurs at a wavelength of 1.742 Å which is near the wavelength of CuK_α radiation (1.542 Å). In this case corrections have to be made to allow for the dispersion of the X-rays that results.

Let $\delta f = |f| - f_o$,

where f_o is the scattering factor without absorption and f is the true scattering factor. It can be shown (James, 1948) that to a good approximation

$$\delta f = \Delta f'_K + \frac{\frac{1}{2}(\Delta f_K'')^2}{f_o + \Delta f'_K}$$

where $\Delta f'_K$ and $\Delta f''_K$ can be calculated from Hönl's theory. $\Delta f'_K$ is independent of the scattering angle whereas the second term is slightly dependent on this angle. The second term is much less important than the first term, and was neglected in the present work

so that the correction to the scattering curve is given by:

$$\delta f = \Delta f'_K = -1.72$$

The values of $\Delta f'_K$ and $\Delta f''_K$ are listed by James (1948).

It can be appreciated that the effect is insensitive to changes in temperature, as the K electrons are far removed from the periphery of the atom.

(C) Structure Determination.

A flow diagram of the course of analysis is shown in Table III.

The second structure factor calculation was carried out on the positions of the iron and chlorine atoms. The position of an atom (x', y', z') related by pseudo-symmetry to an atom (x, y, z) was derived by the following relationships:

$$x' = x + \tfrac{1}{2}$$

$$y' = -y$$

$$z' = z$$

The calculation showed a discrepancy of 57.2%, an exceptionally high value considering the amount of scattering material located. A Fourier synthesis

TABLE III

3-D Patterson Map

↓

Position of Fe atoms

↙ ↘

S.F.I. (Fe atom) R = 73%

Fourier I

Superposition of P(UVW) on Fe positions

↘ ↙

Position of Cl atoms

↓ Fe + 4 Cl atoms ($P2_1/a$)

S.F. II (B_θ = 4, R = 57.2%)

Fourier II (2,164 terms)

↓ (24 of 28 light atoms located in 1 molecule)

S.F. III (B_θ = 4, R = 40.3%)

Fourier III (2,237 terms)

↓ Reduction of symmetry to $P2_1$
(2 Fe, 8 Cl + 49 light atoms as carbon)

S.F. IV (B_θ = 4.55, R = 32.9%)

Fourier IV (2,580 terms)

↓ (2 Fe, 8 Cl, 12 O, 39 C)

S.F. V (B_θ = 4.35, R = 27.8%)

Fourier V

↓ All atoms

S.F. VI (B_θ = 4.65, R = 25.5%)

Fourier VI

↓ All atoms

- Cont'd -

TABLE III. (Cont'd.)

S.F. VII (B_θ = 4.65, R = 24.7%)

Fourier VII (F_o and F_c syntheses)

↓ Omitting two carbon atoms from 1 molecule

S.F. VIII (Individual B_θ, R = 22.7%)

Fourier VIII (F_o and F_c syntheses)

↓ All atoms

S.F. IX (Individual B, R = 22.0%)

Fourier IX (F_o and F_c syntheses)

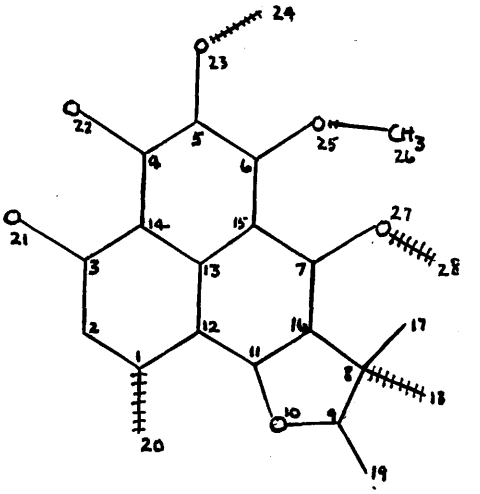
↓ All atoms

Final Structure Factor Calculation (Individual B_θ, R = 21.4%

Final F_o map.

was computed with 2,164 reflexions (the terms in the hOℓ zone with h odd are included in this number).

From this Fourier map, the picture of the molecule emerged fairly clearly (IV). There was no gross disorder in the organic part of the structure, and it appeared that the aromatic nucleus, at least, occupied very closely the sets of positions related by a pseudo glide plane along the a- axis. The molecular structure was apparent from this map, although some atomic positions outwith the nucleus remained in doubt (probably the pseudo symmetry operation does not apply in these cases). The atoms C(18), C(20), C(24), and C(28) could not be precisely located but their presence in the chemical positions shown was evident. The



(IV)

oxygen atoms came up to an average peak height of about 4.0 electrons/A^3, and the carbon atoms came up to peak heights from 2.0 - 3.5 electrons/A^3. There were only

two other peaks in the map, apart from one obvious diffraction ripple, that came up to a height greater than 2 electrons/A^3. These disappeared in subsequent cycles.

A third cycle of structure factor calculations including the twenty four light atoms located in the second Fourier map as carbon atoms, and the iron and four chlorine atoms reduced the R-factor to 40.3%. A Fourier map was computed, with the phases calculated from these atomic positions, omitting 145 reflexions. All the atoms included in the previous cycle came up to satisfactory heights, and the four atoms not included in the previous cycle of calculations were located in this map and confirmed the structure of the atrovenetin derivative as that shown in (IV).

Up to this stage in the analysis, all calculations have led to a mean structure corresponding with a one-molecule asymmetric unit.

(D) Refinement and Destruction of the Pseudo Symmetry.

In order to reduce the symmetry to that of the space group $P2_1$, it was decided to calculate structure factors on all the atoms in one molecule, and omit C(17'), C(18'), C(24'), C(26'), and C(28') from the other molecule. (From this stage, an atom corresponding to, for example, C(4) in the second molecule will be referred to as C(4').) On closer examination, it was thought that there was some doubt about the true position of C(19) and this atom was omitted from both molecules.

This calculation gave a discrepancy of 32.9%, and all the terms were included in the Fourier synthesis. In this map, all atoms came up to satisfactory heights except C(24'), C(26'), and C(28') of the molecule related by pseudo symmetry. These were omitted from the next calculation. The atom C(19) came up to a satisfactory height in both molecules, in positions closely related by pseudo-symmetry. The peak representing C(9), however, was definitely elongated over a region of about 1.2 Å in the x- direction. This could indicate a deviation of the order of 0.4 Å in atomic positions from the positions related by the pseudo glide plane.

This atom, C(9), is an asymmetric centre and reflexion (with or without translation) would form the enantiomorphous structure in the position related by reflexion. This is, of course, impossible as such a symmetry operation produces effectively a different compound. Superposition of the two structures would be impossible. Superimposing the true asymmetric atrovenetin molecule on the position generated by the pseudo space group $P2_1/a$ for this molecule would only involve differences in the positions of the atoms in the five-membered ether ring, particularly C(19), and possibly the methyl groups attached to the oxygen atoms (Fig.III(a)). The carbon atom, C(9), is free to rotate so as to bring C(19) nearer to the position the enantiomorphous C(19) would occupy. These deviations from the space group sites for C(9) and C(19) are probably the major factors in the deviation from the space group $P2_1/a$, together with the slightly different positions occupied by C(17) and C(18'), and C(18) and C(17') respectively. The methyl ether groups also probably deviate from the positions related by pseudo symmetry.

A further cycle of calculations was carried out omitting the atoms C(9), C(9'), C(24'), C(26') and C(28').

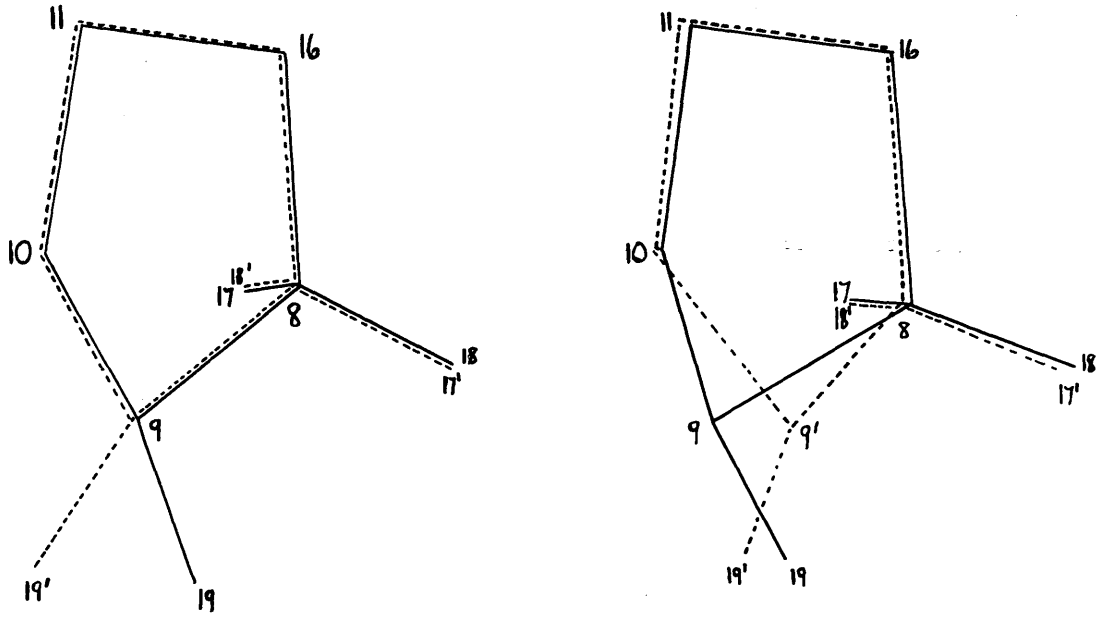


FIG. III.

(A) (B)

A) Shows the superposition of the five-membered ether ring of atrovenetin (unbroken line) on the position afforded for it by the pseudo glide plane (broken line).

B) Shows the conformation adopted by the five-membered ring (unbroken) and the corresponding position afforded by the pseudo space group (broken line).

This succeeded in reducing the R- factor to 27.8%, and confirmed the attenuated nature of the peaks representing C(9) and C(9'). The atoms C(9) and C(9') could then be included at two quite distinct positions for each molecule, which differ considerably from the positions related by the pseudo glide plane. Slight differences in the positions of the methyl groups attached to the oxygen atoms were also noted. Two further cycles of refinement, including all atoms, succeeded in reducing the R- factor to 24.7%, the second of the Fourier syntheses being computed with both $|F_o|$ and $|F_c|$ as the Fourier coefficients. Examination of the peak heights from both syntheses allowed individual isotropic temperature factors to be applied to various types of atom.

A further structure factor calculation was carried out, omitting two atoms, C(24') and C(28'), as they came up to considerably lower heights in the F_o map than in the F_c map. It was hoped that this would further destroy the effects of pseudo symmetry. This calculation showed a discrepancy of 22.7%. A difference map on the output from this calculation indicated slight shifts in these atomic positions, and a further cycle of structure factor calculations including both C(24') and C(28')

and a difference map showed a discrepancy of 22.0%, but no significant alteration in atomic positions.

Owing to the number of atoms involved (66), the structure cannot be refined by a least squares technique on the DEUCE computer, where the upper limit is 64 atoms.

Individual isotropic temperature factors (Table IV) were employed in the final structure factor calculation. The final discrepancy between observed and calculated structure amplitudes is 21.4% and the final values of $|F_o|$, $|F_c|$ and α are listed in Table V.

TABLE IV.

Isotropic Temperature Factors (B_θ).

	Mol.I.	Mol.II.		Mol.I.	Mol.II
C(1)	4.90	4.90	C(18)	4.48	4.48
C(2)	4.55	4.55	C(19)	4.72	4.42
C(3)	4.68	4.68	C(20)	4.68	4.72
C(4)	4.72	4.72	O(21)	5.25	5.25
C(5)	4.78	4.42	O(22)	5.15	5.15
C(6)	4.42	4.42	O(23)	5.15	5.15
C(7)	4.68	4.68	C(24)	4.42	4.55
C(8)	4.42	4.48	O(25)	5.15	4.90
C(9)	4.42	4.55	C(26)	4.68	4.68
O(10)	5.15	5.15	O(27)	4.90	4.90
C(11)	4.90	4.72	C(28)	4.42	4.42
C(12)	4.68	4.48	Fe	4.75	4.75
C(13)	4.42	4.42	Cl(1)	6.00	6.00
C(14)	4.37	4.42	Cl(2)	6.00	6.00
C(15)	4.68	4.68	Cl(3)	5.50	5.50
C(16)	4.72	4.72	Cl(4)	6.00	5.75
C(17)	4.42	4.55			

TABLE V.

h	k	ℓ	$\|F_o\|$	$\|F_c\|$	α
0	0	2	30	17	0
		4	109	100	0
		6	56	49	180
		8	19	3	180
		10	136	122	0
		12	79	80	0
		14	12	8	0
		16	50	50	180
		18	21	21	180
		20	18	21	180
		22	9	0	0
		24	14	14	0
		26	3	3	180
		28	7	1	0
		30	14	9	0
		32	12	17	0
		34	17	16	180
		36	11	12	180
		38	8	6	180
		40	11	11	180
		42	6	7	180
		44	21	21	180
		46	11	11	180
		48	7	9	0
		50	14	14	180
		52	16	18	180
		54	6	5	180
		56	12	12	180
		58	6	7	180
		60	14	14	180
		62	7	10	180
		64	10	13	180
		66	5	5	180
		68	10	10	180
		70	5	5	180
		72	13	15	180
		74	5	5	180
		76	13	13	180
		78	11	12	180
		80	5	5	180
		82	10	10	180
		84	5	5	180
		86	10	10	180
		88	5	5	180
		90	10	10	180

TABLE V. (Cont'd)

h	k	l	$\|F_o\|$	$\|F_c\|$	α
10	3	1	10	27	98
		2	31	41	273
		3	10	12	182
		4	6	5	197
		5	2	9	130
		6	20	22	261
		7	23	29	87
		8	26	30	101
		9	13	15	277
		10	20	25	273
11	3	-10	2	7	39
		-9	10	7	37
		-8	7	4	181
		-7	29	24	208
		-6	11	10	147
		-5	27	23	1
		-4	3	9	321
		-3	11	20	195
		-2	16	11	150
		-1	13	22	197
		0	13	15	186
		1	14	7	340
		2	10	8	325
		3	22	30	178
		4	15	28	3
		5	8	2	295
		6	9	12	65
		7	3	14	0
12	3	-12	17	17	250
		-11	23	19	269
		-10	6	15	102
		-9	10	5	181
		-8	3	8	0
		-7	8	7	301
		-6	26	24	77
		-5	7	5	265
		-4	17	9	266
		-3	7	13	256
		-2	19	24	83
		-1	18	14	108
		0	12	12	283
		1	2	10	104
		2	18	11	104
		3	17	22	74
		4	7	11	75
		5	29	37	272
		6	7	9	94
		7	26	30	75
		8	8	9	268
		9	11	14	7
13	3	-11	10	4	19
		-9	7	20	17
		-8	7	4	15
		-7	21	15	166
		-6	24	32	167
		-5	13	22	15
		-4	11	3	261
		-3	12	16	36
		-2	14	22	4
		-1	5	1	0
		0	12	15	173
		1	21	24	171
		2	11	12	108
		3	8	2	157
		4	20	23	334
		5	8	3	17
		6	8	2	124
		7	15	18	99
14	3	-12	11	6	266
		-11	16	18	99
		-10	6	2	334
		-9	13	19	267
		-8	5	4	56
		-7	8	3	324
		-6	8	8	354
		-5	6	7	99
		-4	5	1	276
		-3	8	7	98
		-2	18	17	103
		-1	5	5	256
		0	16	15	261
		1	12	14	271
		2	39	36	104
		3	13	22	180
		4	24	24	261
		5	8	1	315
		6	11	12	180
		7	11	13	256
		8	3	9	109
		9	10	11	7
15	3	0	11	5	21
		1	7	5	35
		2	11	12	180
		3	3	5	333
		4	4	3	133
		5	3	3	59
		6	5	5	231
		7	5	5	203
		8	3	7	257
16	3	-9	13	7	257
		-8	7	4	98
		-7	22	24	268
		-6	26	26	96
		-5	18	21	274
		-4	13	7	115
		-3	11	17	251
		-2	10	15	3
		-1	16	16	185
		0	13	11	98
		1	19	16	266
		2	10	8	276
		3	15	20	74
		4	17	15	280
0	4	0	10	4	94
		1	38	41	17
		2	18	18	182
		3	29	28	180
		4	53	35	358
		5	32	35	9
		6	7	10	198
		7	24	27	16
		8	10	14	192
		9	14	19	192
		10	12	10	17
		11	7	7	232
1	4	-16	14	11	0
		-15	19	20	260
		-14	28	24	104
		-13	45	52	101
		-12	65	64	270
		-11	7	5	144
		-10	24	18	100
		-9	11	11	192
		-8	6	11	7
		-7	68	65	94
		-6	33	31	255
		-5	34	22	225
		-4	14	17	171
		-3	14	19	228
		-2	41	69	89
		-1	32	19	260
		0	142	142	0
		1	27	29	100
		2	106	99	269
		3	68	75	265
		4	66	70	86
		5	27	28	107
		6	18	22	281
		7	16	18	52
		8	20	20	96
		9	21	21	278
		10	17	25	277
		11	14	14	267
		12	22	21	100
		13	7	6	74
2	4	-16	7	8	1
		-15	8	1	279
		-14	7	5	36
		-13	7	9	167
		-12	15	11	188
		-11	12	12	146
		-10	25	25	13
		-9	20	13	172
		-8	7	1	7
		-7	16	16	14
		-6	5	4	58
		-5	34	22	184
		-4	39	31	3
		-3	24	23	142
		-2	36	34	7
		-1	22	20	13
		0	38	38	97
		1	23	24	31
		2	26	24	132
		3	5	2	88
		4	13	13	147
		5	34	36	15
		6	22	20	119
		7	14	13	269
		8	3	3	70
		9	23	27	350
		10	28	28	355
3	4	-15	14	9	272
		-14	33	28	97
		-13	9	6	159
		-12	11	12	105
		-11	7	11	93
		-10	35	34	256
		-9	23	27	256
		-8	13	16	17
		-7	13	16	108
		-6	7	2	92
		-5	33	33	91
		-4	27	33	279
		-3	106	102	266

h	k	l	$\|F_o\|$	$\|F_c\|$	α
3	4	-2	47	48	99
		-1	3	7	206
		0	3	10	145
		1	54	55	274
		2	30	44	121
		3	50	39	86
		4	48	44	266
		5	76	76	264
		6	79	90	94
		7	22	33	98
		8	14	18	273
		9	16	13	74
		10	21	24	113
		11	12	12	316
		12	10	10	147
		13	10	10	93
4	4	-14	7	7	120
		-13	14	7	
		-12	28	20	157
		-11	20	16	171
		-10	13	17	0
		-9	7	5	304
		-8	12	13	45
		-7	10	5	147
		-6	31	19	161
		-5	4	4	0
		-4	13	5	324
		-3	75	77	177
		-2	28	27	189
		-1	40	39	354
		0	174	174	0
		1	41	40	0
		2	15	16	156
		3	6	2	179
		4	18	24	359
		5	12	17	67
		6	20	23	188
		7	8	12	164
		8	23	28	12
		9	26	37	276
		10	15	10	343
		11	5	8	70
		12	2	6	11
5	4	-15	9	11	85
		-14	7	9	297
		-13	20	27	274
		-12	22	11	299
		-11	7	7	0
		-10	7	5	247
		-9	13	10	182
		-8	19	17	298
		-7	7	7	143
		-6	19	19	84
		-5	58	53	285
		-4	43	50	270
		-3	86	93	87
		-2	67	68	97
		-1	52	49	284
		0	62	61	277
		1	29	21	94
		2	31	46	107
		3	49	49	285
		4	35	39	270
		5	64	77	100
		6	46	57	82
		7	36	40	254
		8	10	10	234
		9	7	9	226
		10	10	15	105
6	4	-16	10	6	209
		-14	7	7	18
		-13	14	5	341
		-12	12	5	157
		-11	5	1	1
		-10	11	3	123
		-9	11	9	215
		-8	19	16	174
		-7	23	23	187
		-6	13	5	0
		-5	48	50	358
		-4	24	13	159
		-3	33	37	197
		-2	2	5	201
		-1	10	22	174
		0	2	15	108
		1	15	15	189
		2	3	7	236
		3	4	35	42	0
		4	5	28	30	177
		5	7	7	14	234
		6	8	13	147
7	4	-14	15	17	277
		-13	7	7	273
		-12	27	21	88
		-11	11	15	100
		-10	7	7	297
		-9	17	17	296
		-8	12	13	142
		-7	7	7	100
		-6	29	23	263
		-5	37	34	275
		-4	69	94	102
		-3	58	70	91
		-2	70	83	265
		-1	40	36	278
		0	22	22	98
		1	33	47	75
		2	14		0
		3	17	11	351
		4	10	20	113
		5	13	13	250
		6	27	32	294
		7		6	269
		8	14	15	52
8	4	-12	12	12	189
		-11	14	21	5
		-10	7	7	9
		-9	7	7	98
		-8	10	7	196
		-7	11	10	177
		-6	5	6	176
		-5	36	44	11
		-4	14	11	109
		-3	10	12	0
		-2	18	17	37
		-1	21	16	30
		0	7	7	153
		1	17	23	172
		2	7	7	346
		3	17	19	358
		4	10	11	271
		5	7	7	210
9	4	-13	17	19	95
		-12	14	15	90
		-11	24	25	274
		-10	24	26	277
		-9	15	10	68
		-8	23	25	99
		-7	15	5	306
		-6	16	21	274
		-5	7	7	344
		-4	7	7	132
		-3	12	17	86
		-2	7	7	10
		-1	15	22	298
		0	12	14	291
		1	7	7	53
10	4	-14	7	7	155
		-13	16	14	188
		-12	7	1	16
		-11	7	6	358
		-10	14	15	346
		-9	19	14	177
		-8	12	4	358
		-7	7	7	196
		-6	11	10	166
		-5	12	11	366
		-4	7	7	14
		-3	15	9	340
		-2	3	4	0
		-1	10	10	184
		0	16	16	272
		1	12	18	294
11	4	-10	29	25	87
		-9	32	34	34
		-8	14	17	310
		-7	14	15	309
		-6	7	7	331
		-5	11	18	177
		-4	23	24	291
		-3	26	24	70
		-2	7	7	59

h	k	l	$\|F_o\|$	$\|F_c\|$	α
11	4	2	7	12	277
		3	7	7	155
		4	7	7	47
		5	7	7	204
		6	24	33	98
		7	10	10	86
		8	19	26	269
		9	9	9	263
		10	7	7	9
		11	12	7	91
		12	11	12	802
12	4	-12	12	7	309
		-11	7	7	206
		-10	11	6	298
		-9	7	7	276
		-8	7	7	217
		-7	22	21	109
		-6	6	8	330
		-5	23	24	191
		-4	11	11	198
		-3	10	7	367
		-2	7	7	196
		-1	27	40	166
		0	14	14	14
		1	13	8	217
		2	7	7	192
		3	10	5	36
		4	5	5	334
		5	28	27	189
		6	29	40	354
		7	10	10	174
		8	21	40	0
		9	2	6	156
		10	2	2	179
		11	6	2	359
		12	7	7	298
13	4	-11	17	16	99
		-10	7	7	174
		-9	7	7	261
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		-7	7	4	235
		-6	7	7	309
		-5	7	7	270
		-4	7	7	298
		-3	12	15	5
		-2	7	6	64
		-1	26	37	276
		0	15	12	269
		1	7	8	70
		2	42	54	93
		3	28	31	279
		4	16	17	274
		5	15	15	89
		6	11	11	95
		7	7	7	267
		8	8	7	94
		9	23	4	136
		10	7	3	166
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		-3	21	18	340
		-2	17	16	20
		-1	7	7	200
		0	14	8	196
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		-5	4	10	12	96
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		1	10	7	285
		2	10	7	92
		3	7	5	201
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		7	15	15	98
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		10	7	7	31
		11	27	21	103
		12	19	25	275
		13	8	5	166
		14	7	7	177
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		2	7	7	79
		3	17	15	79
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		2	7	7	232
		3	4	115	115	358
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		3	7	7	331
		4	7	7	258
11	5	-12	7	7	103
		-11	9	13	103
		-10	7	7	191
		-9	7	7	344
		-8	7	7	266
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		14	7	7	196
		15	7	7	196
7	6	-12	14	13	174
		-11	11	2	4
		-10	14	16	77
		-9	8	14	198
		-8	28	26	175
		-7	42	41	354
		-6	9	14	30
		-5	19	20	200
		-4	9	14	30
		-3	21	13	32
		-2	17	19	196
		-1	19	25	269
		0	16	14	346
		1	7	7	275
		2	7	7	179
		3	7	7	261
		4	7	7	216
		5	7	7	0
		6	7	7	257
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		8	7	7	0
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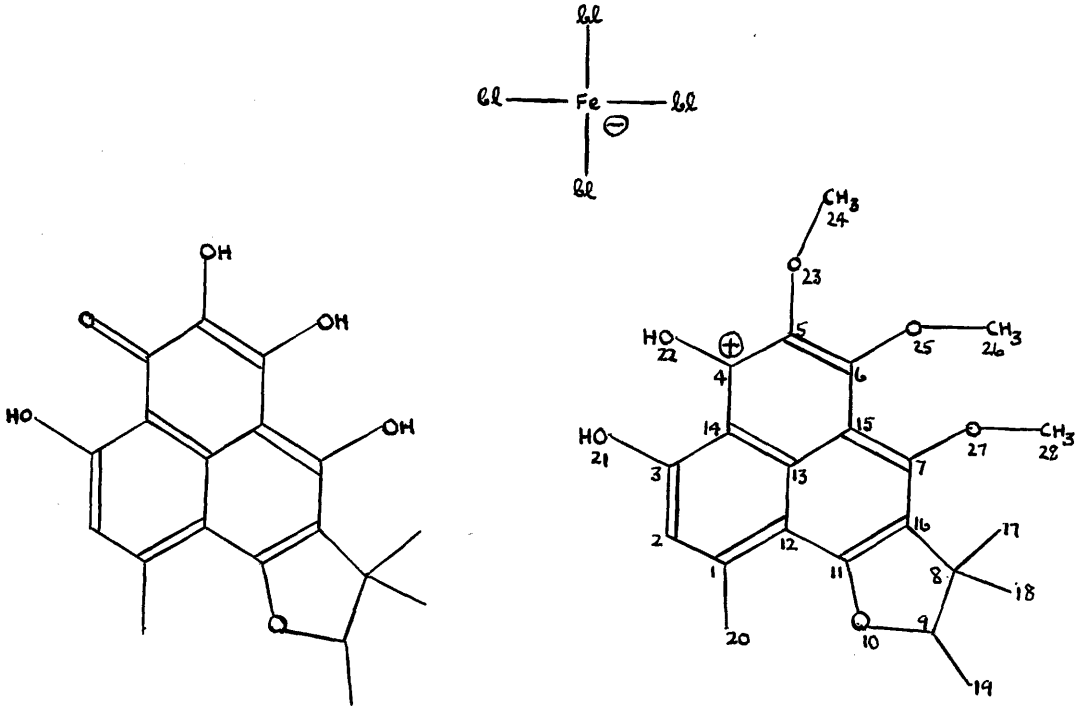
		11	7	7	216
		12	7	7	0
		13	7	7	257
		14	7	7	216
		15	7	7	0
8	6	-12	12	12	2
		-11	16	17	173
		-10	44	34	196
		-9	8	12	21
		-

Conclusions and Discussion:

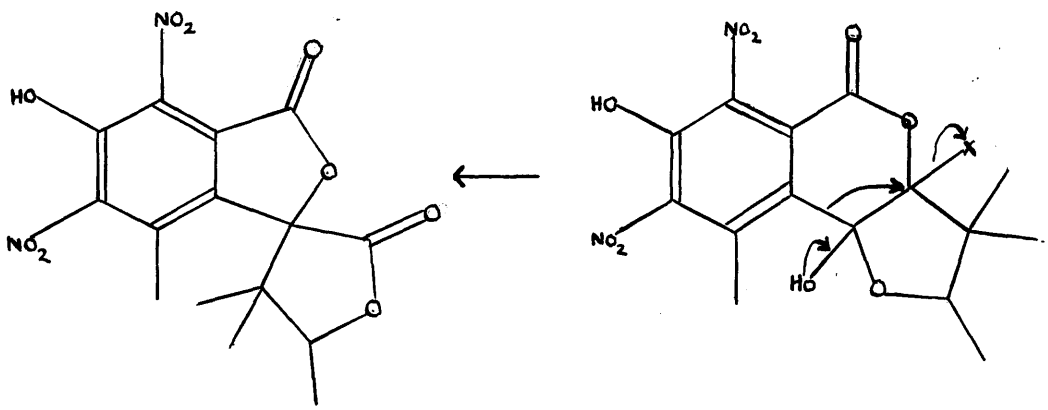
The structure of atrovenetin and the ferrichloride of atrovenetin trimethyl ether (Orange) have been shown to be (V) and (VI) respectively:



(V) (VI)

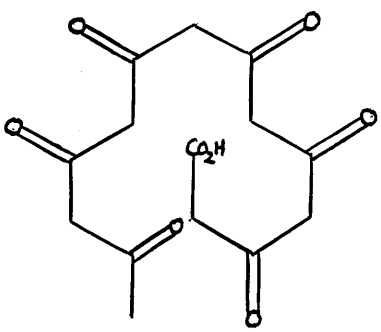
For atrovenetin, various tautomeric structures can be written, while the positive charge on the cation of the ferrichloride is not situated solely on C(4) but distributed over a number of centres. The numbering system adopted is that given by Patterson, Capell, and Walker (1960) for e.g. 7H-Phenaleno- 2,1-d oxazole, up to O(10), and thereafter it is arbitrary.

The structure of atrovenetin differs from that (I) proposed by Barton, de Mayo, Morrison, and Raistrick (1959) in the mode of attachment of the five-membered ether ring. Neill and Raistrick (1957) had oxidised atrovenetin with nitric acid and obtained a compound of the formula $C_{15}H_{14}O_9N_2$ for which Barton, de Mayo, Morrison, and Raistrick proposed structure (VII) and characterised it by N.M.R. spectroscopy. These workers now consider that structure (VII) is formed by rearrangement of (VIII) which is the primary oxidation product of nitric acid on atrovenetin. This rearrangement invalidates the conclusions drawn by Barton and co-workers on the mode of attachment of the ether ring in atrovenetin.

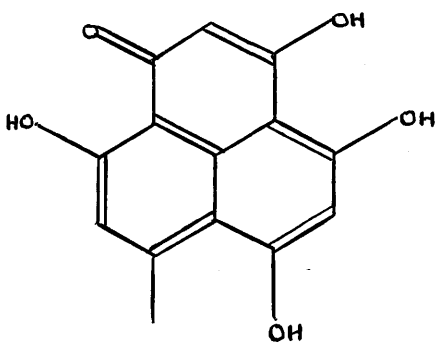


(VII) (VIII)

The structure (V) for atrovenetin is to be preferred biogenetically to (I) as the proposed precursor of the poly-β-diketone type (IX) would form a nucleus (X) with an oxygen atom in the position of the oxygen atom of the five-membered ring.



(IX)



(X)

The structure proposed (II) by Barton, de Mayo, Morrison and Raistrick (1959) for the 'orange' trimethyl ether is correct if allowance is made for the error in assignment of the atrovenetin structure.

Any detailed discussion of the crystal and molecular structure must be dominated by the problem of pseudo-symmetry. This prevents a precise solution of the structure unless the exact extent of the pseudo symmetry can be defined. Although the overall discrepancy is 21.4%, that for the h0ℓ zone of

reflexions is 29.7%, indicating that the exact extent of the deviation from the space group $P2_1/a$ has not been determined. This lack of precision in determining atomic co-ordinates accounts for the high R-factor in this structure. A somewhat similar situation pertains in the crystal structure of Cephalosporin C (Hodgkin and Maslen, 1961). In this case detailed refinement has proved difficult and a recent communication from the Oxford group indicated that refinement is still progressing very slowly even with the aid of least squares procedures.

The final three-dimensional Fourier map is shown in Fig. IV as superimposed contour levels drawn parallel to (010). It shows the two molecules related by the pseudo-glide plane and indicates that the principal deviations from the space group $P2_1/a$ occur in the region of the five-membered ether ring and at the methyl ether groups. The atomic co-ordinates found for the two molecules are listed in Table VI. It can be seen that the greatest deviations from the positions related by the pseudo glide plane occur at C(9), C(17), C(18), C(24), C(26), and C(28). There are other deviations but they can probably be attributed to imprecise location of atomic sites rather than systematic deviation from

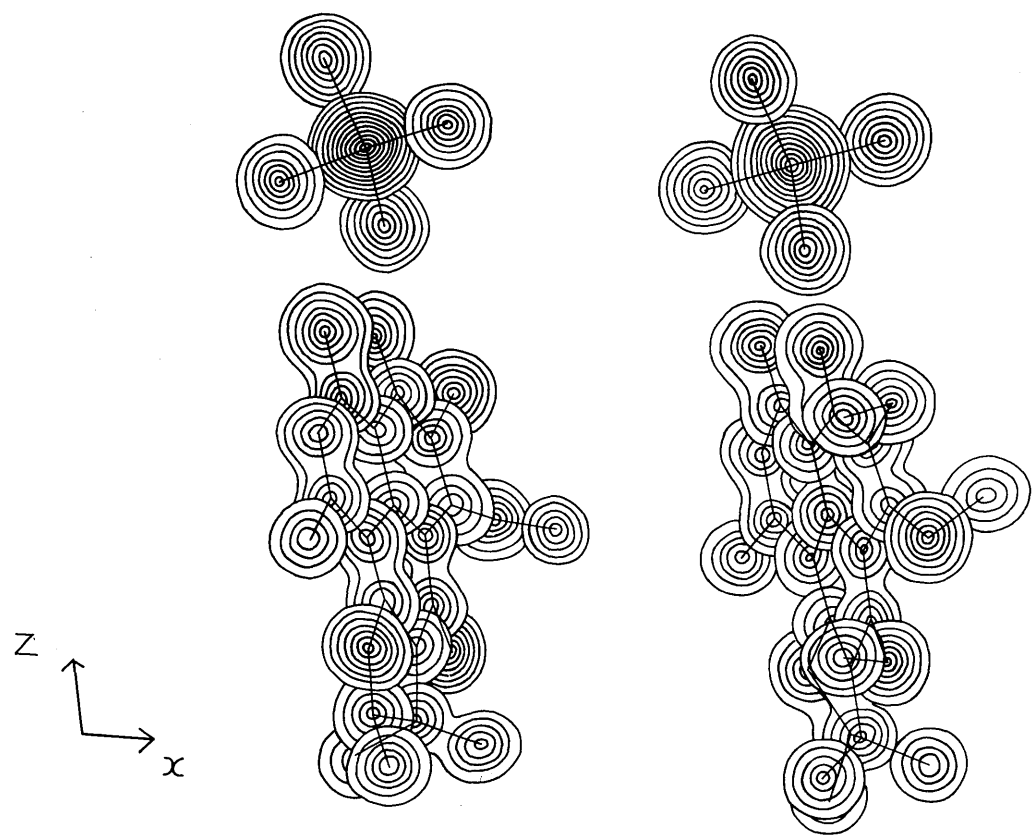


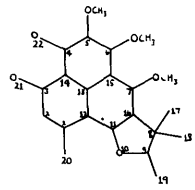
Fig. IV. The final three-dimensional Fourier map, showing the two independent molecules of atrovenetin as superimposed contour sections drawn parallel to (010). Contours are drawn at 1 electron/A^3 intervals, starting at 2 electrons/A^3. In the ferrichloride group, the interval is 3 electrons/A^3.

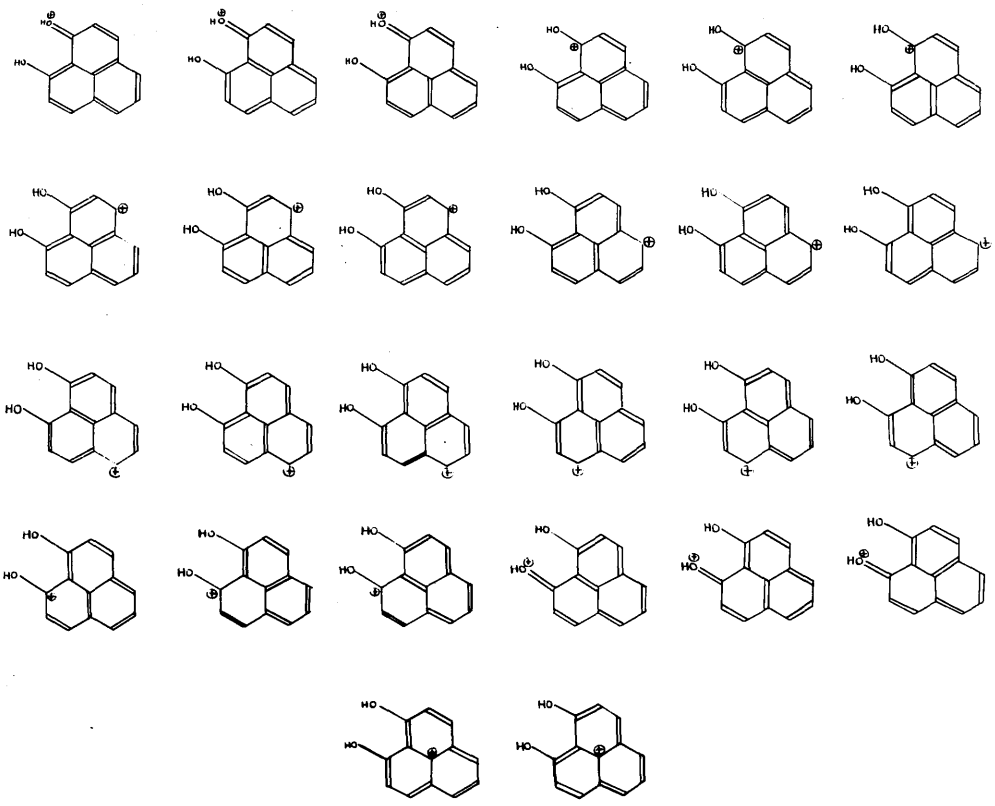
positions related by pseudo symmetry. It does seem therefore that the ferrichloride group and the planar part of the organic structure occupy very closely the positions generated by the pseudo space group $P2_1/a$, whilst the non-planar part of the organic structure, which must necessarily deviate from these positions, adopts a conformation (Fig.III(b)) which allows the minimum deviation. The precise location of these sites is hindered by the fact that there is a strong tendency to average the two slightly-differing sites, and only by successfully determining the phases of the $hO\ell$ terms when h is odd would definite positions for the atoms be achieved. This effect can be seen in the lists of bond lengths (Table VII) and bond angles (Table VIII), where the value for a dimension in one molecule is greater than expected and the value in the related molecule is less than expected.

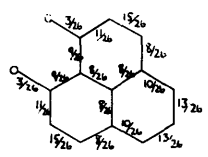
The positions found for the atoms give reasonable agreement with the observed intensities, but do not allow accurate assignment of molecular dimensions to be made. The mean C - C bond length in the aromatic part of the molecule is 1.40 Å with a root mean square deviation of 0.06 Å; the other C - C bond lengths are much less reliable on account of the pseudo symmetry.

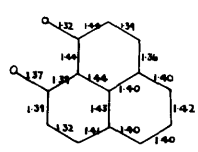
The variations in bond length within the aromatic system can be given some explanation by considering the various possible resonance structures for the trimethyl ether cation (Fig.V). In this treatment, all the possible resonance structures are given unit weight, which is clearly an over-simplification. Furthermore, in this explanation, it is implied that the atrovenetin trimethyl ether cation is symmetrical about the C(13)-C(14) bond. This symmetry is, of course, destroyed by the presence of the various substituents at C(1), C(5), C(6), C(7), C(16), and C(11). Despite these limitations, some correlation can be obtained between the degree of double bond character and observed bond length. In Fig.V the bond lengths averaged over the four 'half-molecules' are plotted against the number of resonance structures that contain double bonds. A more rigorous theoretical treatment is not justified on account of the inaccuracies in the measured bond lengths.

The mean Fe^{III}- Cl distance in the ferrichloride group is 2.17 Å, with a root mean square deviation of 0.05 Å. Penfold and Grigor (1959) find the Fe^{II}- Cl distance in iron (II) chloride tetrahydrate to be 2.38 Å, with the ligands grouped around in the iron atom in distorted octahedra. The sum of the ionic radii for









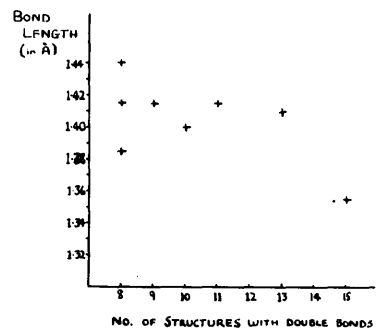

BOND
LENGTH
(in Å)
1·44
1·42
1·40
1·38
1·36
1·34
1·32
8
9
10
11
12
13
14
15
NO. OF STRUCTURES WITH DOUBLE BONDS

FIG. V.

iron (II) and chlorine is 2.56 Å (referred to octahedral co-ordination), while that for iron (III) and chlorine is 2.41 Å. A further correction to this last distance has to be made to allow for the contraction in ionic radius of iron (III) when changing from octahedral to tetrahedral co-ordination. The sum of the ionic radii for a Fe^{III} - Cl bond in tetrahedral co-ordination would then be 2.37 Å, which is 0.20 Å larger than that found in the present work. This shortening effect is paralleled in iron (II) chloride tetrahydrate and suggests that the Fe - Cl bonds in both compounds may have some degree of covalent character.

The mean $C(sp^2)$-O bond length is 1.36 Å, which agrees with the value found in salicylic acid (Cochran, 1953), and the mean $C(sp^3)$-O distance is 1.47 Å, which agrees with that found in cyclopentene oxide (Erlandsson, 1955). The short C(4) - O(22) distances may indicate a greater degree of double bond character in this bond than would be suggested by the resonance structures in Fig.V.

Intramolecular non-bonded distances of interest in both molecules are listed in Table IX, while intermolecular contacts less than 4 Å are given in Table X. The packing of molecules projected down the b- axis is shown in Fig.VI.

In addition to the ionic link, it is probable that a hydrogen bond exists between Cl(1) and O(22). The average distance between these atoms is 3.19 Å; this appears slightly longer than the values of 3.07 Å found in D(-) isoleucine hydrochloride monohydrate (Trommel and Bijvoet, 1954) and of 3.12 Å found in adenine hydrochloride (Broomhead, 1948 and Cochran, (1951) for O - H ... Cl hydrogen bonds, although a value of 3.24 Å was also recorded in the isoleucine analysis. The mean value of the angle Cl(1)O(22)C(4) is 131°, which, although much larger than the expected tetrahedral value, does not completely exclude the possibility of hydrogen bond formation.

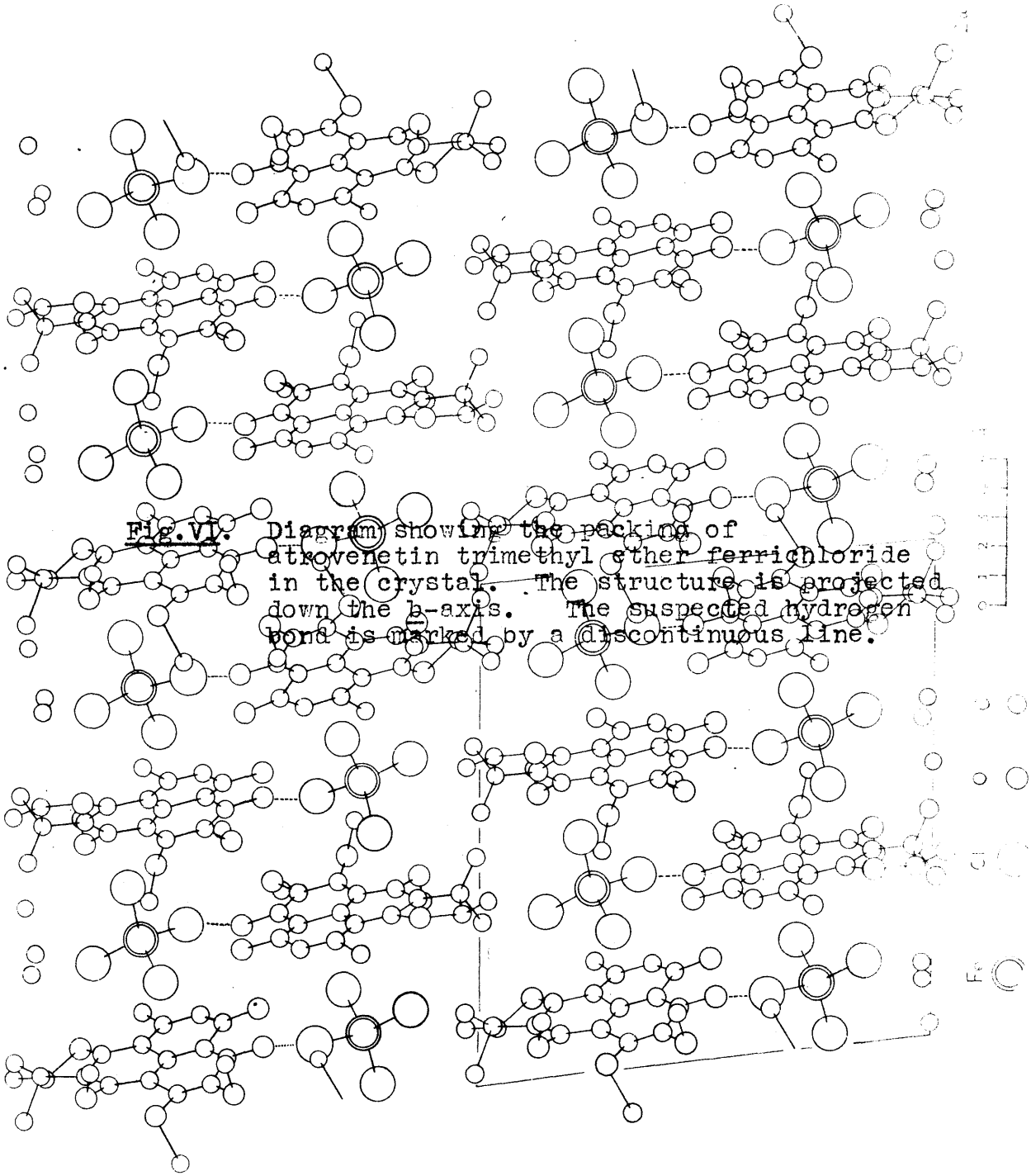


Fig.VI. Diagram showing the packing of atrovenetin trimethyl ether ferrichloride in the crystal. The structure is projected down the b-axis. The suspected hydrogen bond is marked by a discontinuous line.

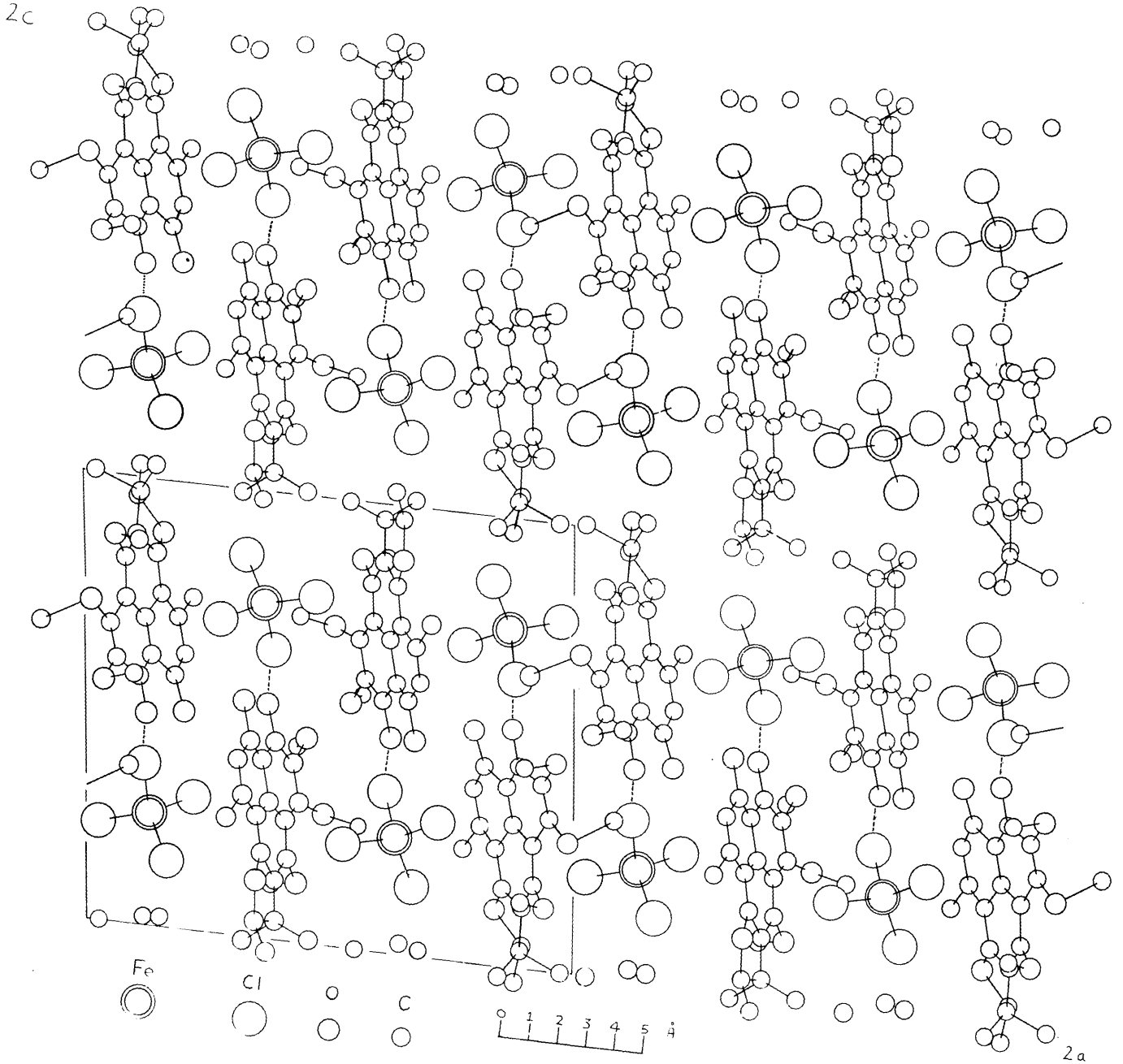

2c
Fe
Cl
O
C
0 1 2 3 4 5 Å
2a

TABLE VI (A).

The atomic co-ordinates for Atrovenetin Trimethyl Ether Ferrichloride. (Molecule I).

	x/a	y/b	z/c
C(1)	0.5160	0.6686	0.3093
C(2)	0.5075	0.6592	0.3895
C(3)	0.5509	0.5455	0.4519
C(4)	0.5928	0.5229	0.4426
C(5)	0.4297	0.2084	0.3993
C(6)	0.4427	0.2258	0.3095
C(7)	0.4156	0.3578	0.1800
C(8)	0.5911	0.4910	0.0405
C(9)	0.5582	0.6299	0.0312
O(10)	0.3405	0.6705	0.1222
C(11)	0.3621	0.5709	0.1796
C(12)	0.5496	0.5619	0.2611
C(13)	0.5785	0.4411	0.3053
C(14)	0.5654	0.4415	0.3970
C(15)	0.4127	0.3504	0.2692
C(16)	0.3889	0.4498	0.1554
C(17)	0.3231	0.4132	-0.0104
C(18)	0.4615	0.4941	0.0057
C(19)	0.3540	0.7502	-0.0238

- Cont'd -

TABLE VI (A). - Cont'd -

The atomic co-ordinates for Atrovenetin Trimethyl Ether Ferrichloride. (Molecule I)

	x/a	y/b	z/c
C(20)	0.2822	0.7997	0.2554
O(21)	0.3198	0.5416	0.5203
O(22)	0.3771	0.3028	0.5251
O(23)	0.4586	0.0931	0.4573
C(24)	0.4256	-0.0463	0.4310
O(25)	0.4907	0.1336	0.2926
C(26)	0.5636	0.1616	0.2753
O(27)	0.4342	0.2315	0.1327
C(28)	0.3824	0.1066	0.1218
Fe	0.3717	0.1825	0.7499
Cl(1)	0.3898	0.0318	0.6501
Cl(2)	0.3345	0.0602	0.8556
Cl(3)	0.2792	0.3307	0.7045
Cl(4)	0.4781	0.2898	0.7789

TABLE VI.(B).

The atomic co-ordinatesfor Atrovenetin Trimethyl Ether Ferrichloride (Molecule II).

	x/a	y/b	z/c
C(1)	0.8152	0.3302	0.3052
C(2)	0.8015	0.3373	0.3882
C(3)	0.8243	0.4582	0.4410
C(4)	0.8875	0.6894	0.4452
C(5)	0.9356	0.7857	0.4089
C(6)	0.9479	0.7753	0.3278
C(7)	0.9152	0.6631	0.1828
C(8)	0.8945	0.5184	0.0356
C(9)	0.8957	0.3461	0.0501
O(10)	0.8440	0.3265	0.1220
C(11)	0.8597	0.4410	0.1698
C(12)	0.8463	0.4347	0.2606
C(13)	0.8767	0.5519	0.3101
C(14)	0.8634	0.5648	0.3955
C(15)	0.9135	0.6659	0.2720
C(16)	0.8925	0.5400	0.1291
C(17)	0.8492	0.6233	-0.0212
C(18)	0.9753	0.5699	-0.0004
C(19)	0.8558	0.2757	-0.0343

- Cont'd -

TABLE VI (B). - Cont'd -

The atomic co-ordinates for Atrovenetin Trimethyl Ether Ferrichloride (Molecule II).

	x/a	y/b	z/c
C(20)	0.7785	0.2060	0.2528
O(21)	0.8034	0.4638	0.5192
O(22)	0.8759	0.6994	0.5245
O(23)	0.9642	0.8854	0.4584
C(24)	0.9033	0.0024*	0.4414
O(25)	0.9878	0.8818	0.2848
C(26)	0.0597*	0.8688	0.3455
O(27)	0.9365	0.7701	0.1518
C(28)	0.8876	0.8859	0.1593
Fe	0.8697	0.8253	0.7489
Cl(1)	0.8814	0.9599	0.6405
Cl(2)	0.8346	0.9383	0.8535
Cl(3)	0.7771	0.6685	0.7022
Cl(4)	0.9767	0.7126	0.7797

* It is necessary to add the full unit cell translation to these co-ordinates to obtain a complete molecule.

TABLE VII.

Bond Distances (in Å).

	Mol.I.	Mol.II.		Mol.I.	Mol.II
C(1) - C(2)	1.28	1.35	C(8) - C(17)	1.52	1.50
C(1) - C(12)	1.44	1.37	C(8) - C(18)	1.37	1.65
C(1) - C(20)	1.59	1.55	C(9) - O(10)	1.47	1.52
C(2) - C(3)	1.32	1.46	C(9) - C(19)	1.35	1.57
C(3) - C(14)	1.32	1.46	O(10) - C(11)	1.34	1.35
C(3) - O(21)	1.42	1.32	C(11) - C(12)	1.32	1.47
C(4) - C(5)	1.48	1.41	C(11) - C(16)	1.48	1.31
C(4) - C(14)	1.40	1.47	C(12) - C(13)	1.42	1.44
C(4) - O(22)	1.36	1.28	C(13) - C(14)	1.48	1.39
C(5) - C(6)	1.46	1.32	C(13) - C(15)	1.37	1.44
C(5) - O(23)	1.49	1.30	O(23) - C(24)	1.50	1.54
C(6) - C(15)	1.27	1.45	O(25) - C(26)	1.33	1.46
C(6) - O(25)	1.26	1.45	O(27) - C(28)	1.50	1.41
C(7) - C(15)	1.40	1.40	Fe - Cl(1)	2.19	2.17
C(7) - C(16)	1.35	1.48	Fe - Cl(2)	2.19	2.12
C(7) - O(27)	1.34	1.38	Fe - Cl(3)	2.19	2.25
C(8) - C(9)	1.62	1.68	Fe - Cl(4)	2.09	2.13
C(8) - C(16)	1.51	1.48			

TABLE VIII.

Bond Angles in Both Molecules.

C(2)	C(1)	C(12)	124°	125°	C(9)	C(8)	C(17)	89°	138°
C(2)	C(1)	C(20)	120°	116°	C(9)	C(8)	C(18)	117°	111°
C(12)	C(1)	C(20)	116°	117°	C(16)	C(8)	C(17)	105°	115°
C(1)	C(2)	C(3)	119°	121°	C(16)	C(8)	C(18)	121°	115°
C(2)	C(3)	C(14)	124°	113°	C(17)	C(8)	C(18)	117°	89°
C(2)	C(3)	O(21)	116°	118°	C(8)	C(9)	O(10)	101°	103°
C(14)	C(3)	O(21)	120°	128°	C(8)	C(9)	C(19)	120°	109°
C(5)	C(4)	C(14)	121°	118°	O(10)	C(9)	C(19)	116°	110°
C(5)	C(4)	O(22)	118°	120°	C(9)	O(10)	C(11)	115°	102°
C(14)	C(4)	O(22)	121°	121°	O(10)	C(11)	C(12)	129°	117°
C(4)	C(5)	C(6)	119°	121°	O(10)	C(11)	C(16)	109°	114°
C(4)	C(5)	O(23)	114°	117°	C(12)	C(11)	C(16)	121°	129°
C(6)	C(5)	O(23)	127°	125°	C(1)	C(12)	C(11)	125°	130°
C(5)	C(6)	C(15)	118°	123°	C(1)	C(12)	C(13)	118°	116°
C(5)	C(6)	O(25)	107°	122°	C(11)	C(12)	C(13)	116°	114°
C(15)	C(6)	O(25)	134°	115°	C(12)	C(13)	C(14)	113°	120°
C(15)	C(7)	C(16)	123°	123°	C(12)	C(13)	C(15)	126°	122°
C(15)	C(7)	O(27)	123°	127°	C(14)	C(13)	C(15)	121°	117°
C(16)	C(7)	O(27)	114°	110°	C(3)	C(14)	C(4)	124°	116°
C(9)	C(8)	C(16)	103°	91°	C(3)	C(14)	C(13)	122°	123°

- Cont'd -

TABLE VIII. - Cont'd -

Bond Angles in Both Molecules.

C(4)	C(14)	C(15)	114°	121°
C(6)	C(15)	C(7)	119°	124°
C(6)	C(15)	C(13)	126°	119°
C(7)	C(15)	C(13)	115°	118°
C(7)	C(16)	C(8)	134°	130°
C(7)	C(16)	C(11)	118°	114°
C(8)	C(16)	C(11)	108°	116°
C(5)	O(23)	C(24)	115°	104°
C(6)	O(25)	C(26)	123°	92°
C(7)	O(27)	C(28)	120°	110°
Cl(1)	Fe	Cl(2)	105°	111°
Cl(1)	Fe	Cl(3)	111°	106°
Cl(1)	Fe	Cl(4)	107°	109°
Cl(2)	Fe	Cl(3)	110°	110°
Cl(2)	Fe	Cl(4)	115°	114°
Cl(3)	Fe	Cl(4)	109°	106°

TABLE IX.

Some Non-bonded Intramolecular Contacts (in Å).

	Mol.I	Mol.II		Mol.I	Mol.II
C(1) ...C(14)	2.68	2.75	O(10)...C(19)	2.40	2.53
C(2) ...C(13)	2.84	2.80	C(11)...C(15)	2.80	2.79
C(3) ...C(12)	2.74	2.90	C(13)...C(16)	2.72	2.88
C(4) ...C(15)	2.78	2.81	C(15)...C(26)	3.04	3.27
C(4) ...C(24)	3.63	3.05	C(15)...C(28)	3.16	2.97
C(5) ...C(13)	2.78	2.86	C(16)...C(28)	3.33	3.36
C(5) ...C(24)	2.52	2.24	C(17)...C(18)	2.47	2.20
C(5) ...C(26)	3.20	2.57	C(17)...C(19)	3.13	3.38
C(6) ...C(14)	2.90	2.78	C(17)...O(27)	3.27	3.02
C(6) ...C(24)	3.28	2.98	C(17)...C(28)	3.69	3.58
C(6) ...C(26)	2.28	2.10	C(18)...C(19)	2.93	3.51
C(6) ...C(28)	3.21	3.19	C(18)...O(27)	3.30	2.97
C(7) ...C(12)	2.80	2.85	C(18)...C(28)	4.45	4.15
C(7) ...C(26)	3.28	3.88	O(21)...O(22)	2.51	2.59
C(7) ...C(28)	2.45	2.30	O(22)...O(23)	2.75	2.64
C(8) ...O(10)	2.38	2.51	O(22)...C(24)	3.82	3.27
C(8) ...C(19)	2.58	2.64	O(23)...O(25)	2.73	2.80
C(8) ...O(27)	2.95	2.91	O(23)...C(26)	3.60	2.55
C(8) ...C(28)	3.94	3.92	O(25)...C(24)	3.09	3.21
C(9) ...C(11)	2.38	2.24	C(24)...C(26)	4.12	3.47
C(9) ...C(16)	2.45	2.25	O(25)...C(28)	3.07	2.68
C(9) ...C(17)	2.20	2.98	C(26)...O(27)	3.02	3.85
C(9) ...C(18)	2.55	2.73	C(26)...C(28)	3.72	4.07

TABLE X.

Intermolecular Contacts (< 4 Å).

(in Å)

The Roman Numerals refer to the following positions:

I.	x,y,z+1	V.	2-x,y+½,$\bar{z}$
II.	x,$\bar{y}$+1,z	VI.	1-x,y+½,$\bar{z}$+1
III.	x,y+1,z+1	VII.	2-x,y+½,$\bar{z}$+1
IV.	1-x,y+½,$\bar{z}$	VIII.	1-x,y-½,$\bar{z}$+1

O(22') .... Cl(1')	3.10	Cl(2') .... C(12)^{VI}	3.63
C(24') .... O(21')^{VII}	3.10	C(24) .... Cl(1)	3.64
C(24') .... Cl(1')	3.21	O(22) .... C(24)^{VI}	3.65
O(22) .... Cl(1)	3.27	C(19) .... O(10')^{IV}	3.66
O(23') .... Cl(1')	3.41	O(21) .... Cl(3)	3.67
O(23) .... Cl(1)	3.42	Cl(3') .... C(15)^{VI}	3.67
O(22') .... Cl(3')	3.43	C(18) .... C(28)^{IV}	3.68
C(11) .... Cl(4)^{VI}	3.45	C(4) .... C(24)^{VI}	3.69
O(22) .... Cl(3)	3.45	C(15') .... Cl(3)^{VI}	3.71
O(10) .... Cl(4)^{VI}	3.48	Cl(2') .... C(19')^{III}	3.71
C(11') .... Cl(2)^{VI}	3.48	Cl(3') .... C(5)^{VI}	3.71
C(18') .... C(19')^{V}	3.49	Cl(4') .... C(18')^{I}	3.71
C(2) .... C(24)^{II}	3.51	Fe .... O(22)	3.72
O(21') .... Cl(3')	3.56	C(4') .... Cl(3)^{VI}	3.72
Cl(4) .... O(25)^{VI}	3.57	C(1) .... C(24)^{II}	3.73
Cl(2') .... C(11)^{VI}	3.57	Fe .... O(22')	3.73
C(9) .... C(19')^{IV}	3.60	Cl(1') .... C(2)^{VI}	3.73
C(12') .... Cl(2)^{VI}	3.60	Cl(3') .... C(13)^{VI}	3.73
O(10) .... C(19')^{IV}	3.61	O(21) .... C(26)^{VI}	3.74
C(18') .... C(9')^{V}	3.61	C(18) .... O(27)^{IV}	3.75
Cl(2') .... C(17')^{I}	3.62	C(26) .... C(20')	3.75

- Cont'd -

TABLE X. - Cont'd -

Intermolecular Contacts (<4 Å).

(in Å)

Cl(4)	....	C(26)^{VI}	3.75	C(14)	....	O(23)^{VI}	3.84
C(2')	....	Cl(1)^{VI}	3.75	O(10')	....	Cl(2)^{VI}	3.84
C(14')	....	Cl(3)^{VI}	3.75	Cl(2')	....	C(16)^{VI}	3.84
Cl(1')	....	C(3)^{VI}	3.75	Cl(3)	....	C(20')^{VI}	3.85
C(20)	....	C(24)^{II}	3.76	Cl(2')	....	C(17)^{VI}	3.86
C(24')	....	C(3')^{VII}	3.77	C(2)	....	O(21')^{VI}	3.87
Cl(3')	....	C(4)^{VI}	3.77	C(6')	....	Cl(3)^{VI}	3.88
Cl(3')	....	C(6)^{VI}	3.77	C(24')	....	O(22')^{VI}	3.88
O(21)	....	O(23)^{VI}	3.78	C(24')	....	Cl(4')^{VI}	3.88
C(13')	....	Cl(3)^{VI}	3.78	O(21)	....	C(2')^{VI}	3.90
C(12)	....	Cl(4)^{VI}	3.79	C(5')	....	Cl(3)^{VI}	3.90
C(20)	....	Cl(3')^{VI}	3.79	C(16')	....	Cl(2)^{VI}	3.91
Cl(2')	....	O(10)^{VI}	3.79	C(28')	....	C(17')^{IV}	3.91
Cl(3')	....	C(14)^{VI}	3.79	C(18)	....	Cl(2)^{VI}	3.93
C(3)	....	O(23)^{VI}	3.82	O(21)	....	C(24')^{VIII}	3.94
C(19)	....	C(19')^{IV}	3.82	C(20)	....	C(19')^{IV}	3.95
C(3')	....	Cl(1)^{VI}	3.82	O(22)	....	O(23)^{VI}	3.95
C(28')	....	C(18')^{V}	3.82	C(15)	....	Cl(1)^{VI}	3.96
C(26)	....	Cl(1)^{VI}	3.83	O(27')	....	C(18')^{V}	3.96
C(4)	....	O(23)^{VI}	3.84				

A P P E N D I C E S.

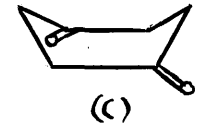
A P P E N D I X I.

Attempts to Solve the Structure of 1:4-cyclohexanedione.

Studies of the Kerr effect and of dipole moments applied to 1:4-cyclohexanedione seem to indicate an unusual conformation for this compound. (Le Fèvre and Le Fèvre, 1935 and 1955). Both chemical and spectroscopic evidence (Silberstein, 1917) definitely rule out the possibility of enolisation in the substance, as is found in diketopiperazine. Le Fèvre interprets his results as indicating a mixture of 80% of conformation (A) and 20% of conformation (C). (I).

(A)

(B)



(C)

(I)

Barton and Cookson (1956) conclude that the successive substitution of trigonal hybridised carbon atoms for

tetrahedrally hybridised carbon atoms will cause a carbocyclic ring to approach planarity. This effect can be traced in cyclohexanone and would be expected to be more pronounced in 1:4-cyclohexanedione.

Hassel (1956) appears to have done some crystallographic work on this compound, but has never published any details of it.

1:4-cyclohexanedione crystallises as small, white needles, which sublime if left for more than a few hours in the atmosphere. This difficulty was overcome by coating the crystals with a plastic solution, 'Gelva'. The preliminary measurements are summarised in Table I.

The space group was not determined uniquely by the systematic absence of spectra. It could be either $P2_1$ or $P2_1/m$. From a consideration of molecular packing and by examination of the two-dimensional Patterson projection, P(UW) Fig.I., the former seemed the more probable space group. All attempts to solve the structure in its b- axis projection failed, although the probable orientation of the molecule in the unit cell could be determined from the two-dimensional Patterson function. The optical transform method was used extensively at this stage, but lack of success

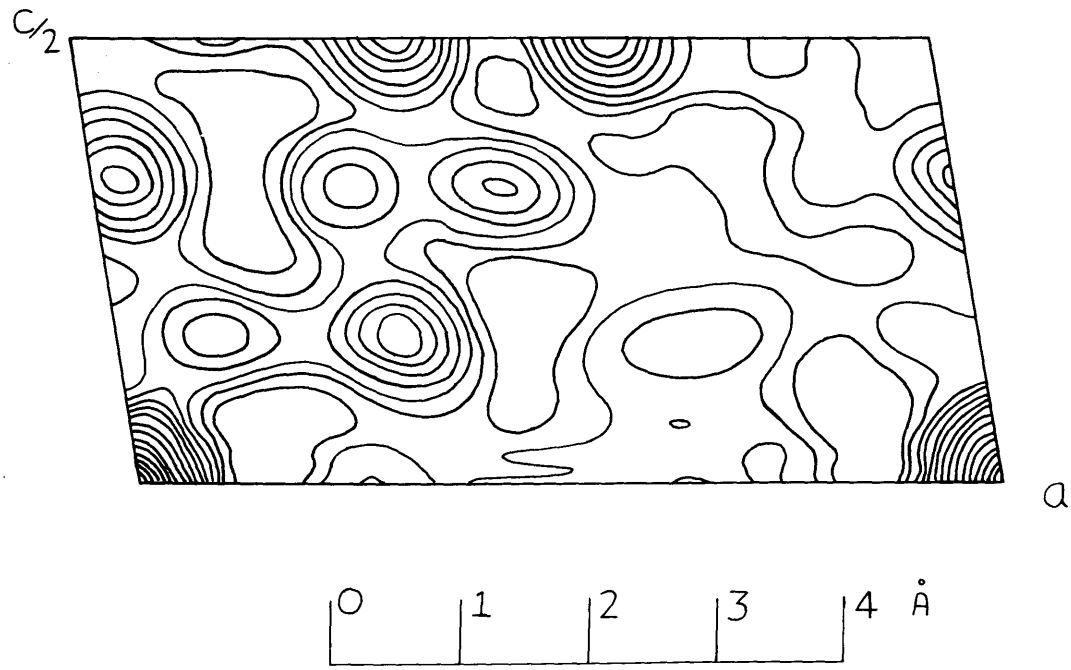


Fig.I. Two-dimensional Patterson projection, P(U,W). Contours are at arbitrary intervals.

can probably be attributed to having only an approximate knowledge of the orentation, and degree of tilt of the molecule.

The measured structure amplitudes are given in Table II.

TABLE I.

Molecular Formula	$C_6H_8O_2$
Molecular Weight (M)	112
d (meas.)	1.20 gm./cc.
d(calc.)	1.24 gm./cc.
Crystal System	Monoclinic
a	6.75 ± 0.04 Å
b	6.40 ± 0.04 Å
c	7.02 ± 0.04 Å
β	$99^{\circ}40'$
Volume of Unit Cell	300.3 $Å^3$
Number of Molecules (Z)	2
Systematic Absences	0k0 when k is odd.
Space Group	$P2_1$ (C_2^2) or $P2_1/m$ (C_{2h}^2)
F(000)	120

TABLE II.

Observed Structure Amplitudes.
(Arbitrary Scale)

H	K	L	$\|F_o\|$	H	K	L	$\|F_o\|$
0	0	2	25.5	2	0	$\bar{5}$	4.8
0	0	3	8.3	2	0	$\bar{4}$	2.7
0	0	4	6.0	2	0	$\bar{3}$	35.7
0	0	6	26.8	2	0	$\bar{2}$	36.3
0	0	7	2.7	2	0	$\bar{1}$	12.2
1	0	$\bar{7}$	2.9	2	0	0	40.2
1	0	$\bar{6}$	5.8	2	0	1	22.8
1	0	$\bar{5}$	3.3	2	0	2	6.4
1	0	$\bar{4}$	2.5	2	0	3	32.4
1	0	$\bar{3}$	21.0	2	0	4	2.1
1	0	$\bar{2}$	21.6	2	0	6	7.1
1	0	$\bar{1}$	67.2	3	0	$\bar{6}$	8.3
1	0	0	29.1	3	0	$\bar{5}$	5.2
1	0	1	16.6	3	0	$\bar{4}$	12.0
1	0	2	10.4	3	0	$\bar{3}$	11.0
1	0	3	27.8	3	0	$\bar{2}$	20.3
1	0	4	4.3	3	0	$\bar{1}$	29.6
1	0	5	25.5	3	0	0	47.3
1	0	7	3.7	3	0	1	16.2

- Cont'd -

TABLE II. - Cont'd -

Observed Structure Amplitudes.

(Arbitrary Scale)

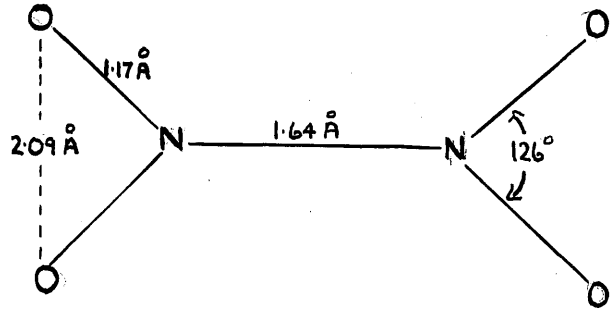
H	K	L	$\|F_o\|$	H	K	L	$\|F_o\|$
3	0	2	21.6	5	0	2	21.8
3	0	4	8.9	5	0	3	2.7
3	0	5	8.7	5	0	4	5.4
3	0	6	6.8	5	0	5	5.0
4	0	$\bar{5}$	4.6	6	0	$\bar{4}$	2.7
4	0	$\bar{4}$	7.9	6	0	$\bar{3}$	8.1
4	0	$\bar{3}$	26.6	6	0	$\bar{2}$	4.8
4	0	$\bar{2}$	3.4	6	0	$\bar{1}$	2.7
4	0	$\bar{1}$	30.3	6	0	0	3.3
4	0	0	11.4	6	0	1	4.2
4	0	1	7.8	6	0	2	2.9
4	0	2	12.3	6	0	3	4.3
4	0	3	22.8	7	0	$\bar{3}$	8.9
4	0	4	4.8	7	0	$\bar{2}$	2.3
4	0	5	9.4	7	0	$\bar{1}$	3.1
5	0	$\bar{4}$	16.4	7	0	0	4.1
5	0	$\bar{3}$	1.7	7	0	1	2.9
5	0	$\bar{1}$	9.3	7	0	3	8.3
5	0	0	6.4	8	0	$\bar{2}$	3.3
5	0	1	2.5	8	0	2	2.9

A P P E N D I X II.

The Crystal Structure of Dinitrogen Tetroxide:

Some further refinement of the data of Broadley and Robertson.

Early work in this department (Broadley and Robertson, 1949, and Broadley, 1950) on the crystal structure of dinitrogen tetroxide had succeeded in showing that the molecule most probably crystallised in the cubic space group Im3. There were six molecules in the unit cell, and as the space group has forty eight general positions the nitrogen and oxygen atoms must occupy special positions. The asymmetric unit of the cell contains one quarter of a nitrogen atom and one half of an oxygen atom and the best agreement with the observed results was obtained when nitrogen was placed at a point (0.394,0,0) and the oxygen at (0.327, 0.134, 0). Broadley and Robertson obtained the intensities of 44 reflexions from photographs of two zones, taken about the principal axis and the body diagonal. An experimental scattering curve was used in the earlier work and the agreement between observed and calculated structure amplitudes was about 16%. The dimensions of the molecule found by Broadley and Robertson are shown in (I).



(I)

Smith and Hedberg (1956) studied dinitrogen tetroxide gas by electron diffraction and they found basically the same structure with the molecular dimensions given in Table I. The remarkable feature of both these analyses is the very long N - N bond which is considerably longer than that of 1.47 Å found in hydrazine (Giguère and Schomaker, 1943). An attractive suggestion of Smith and Hedberg is that the N - N bond is largely a π-bond rather than a σ-bond and this would explain the exceptional length and the chemical weakness on account of the poor overlap of atomic orbitals.

An attempt at further refinement of the data of Broadley and Robertson was made to find if this would indicate any significant alteration in molecular structure. The final co-ordinates obtained by the

earlier workers were refined by the method of least squares. The scattering curves of Berghuis et al (1955) were used for nitrogen and oxygen, starting with an isotropic temperature factor (B_θ) of 3. The initial R-factor for the observed reflexions was 20.3% and after ten cycles of refinement this was reduced to 14.6%, a further cycle of refinement failing to alter either the R-factor or $\Sigma w\Delta^2$. The weighting system employed in the refinement was:

$$\sqrt{w(hk\ell)} = \frac{|F_o(hk\ell)|}{17.8} \quad \text{if } |F_o| < 17.8$$

$$\sqrt{w(hk\ell)} = \frac{17.8}{|F_o(hk\ell)|} \quad \text{if } |F_o| \geq 17.8$$

Anisotropic temperature factors were obtained and indicate only a slight increase of vibration of the oxygen atom in a direction perpendicular to the N - N bond, but in the plane of the molecule. The final co-ordinates and temperature factors are given in Table II.

A Fourier (F_o) synthesis was computed in the plane of the molecule and is shown in Fig. I. This contains some large peaks not accounted for by structural details. A difference Fourier ($F_o - F_c$)

synthesis was computed in the plane of the molecule and this is shown in Fig. II. This indicates that no further significant shifts were to be expected and that the spurious peaks in the F_o synthesis are due to lack of data and termination of series effects. The final molecular dimensions are given in Table I, together with the estimated standard deviation evaluated from least squares residuals. These values suggest that no significant alteration of the results of Broadley and Robertson can be obtained from the number of observations recorded.

The final values of the observed and calculated structure amplitudes are listed in Table III. None of the signs of the structure factors observed by Broadley and Robertson have changed during the course of refinement.

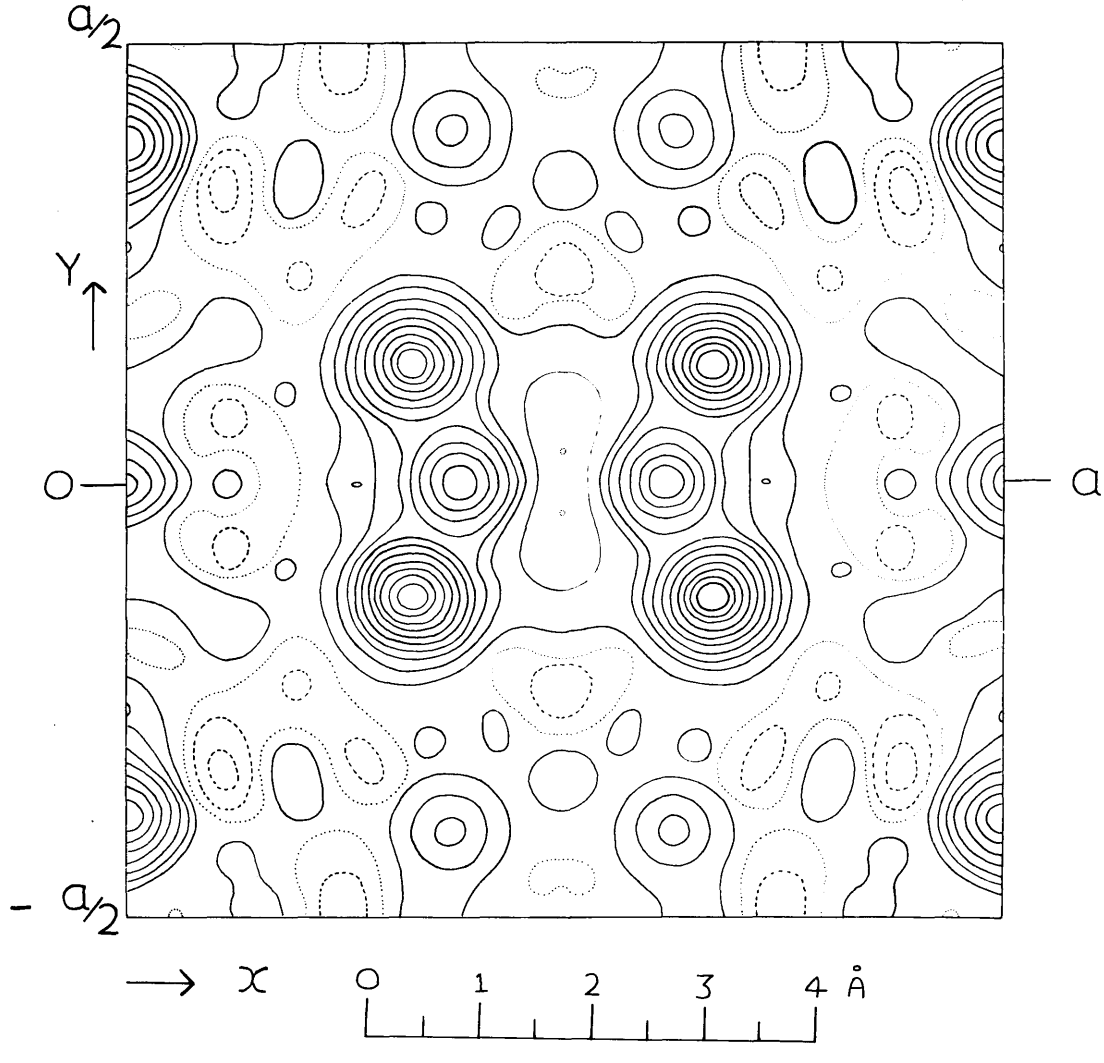


Fig.I. Fourier (F_o) Section (x,y,0), through the plane of the dinitrogen tetroxide molecule. The contours are drawn at intervals of 1 electron/Å^3. The zero contour is represented thus ..... , while negative contours are represented thus - - - - - .

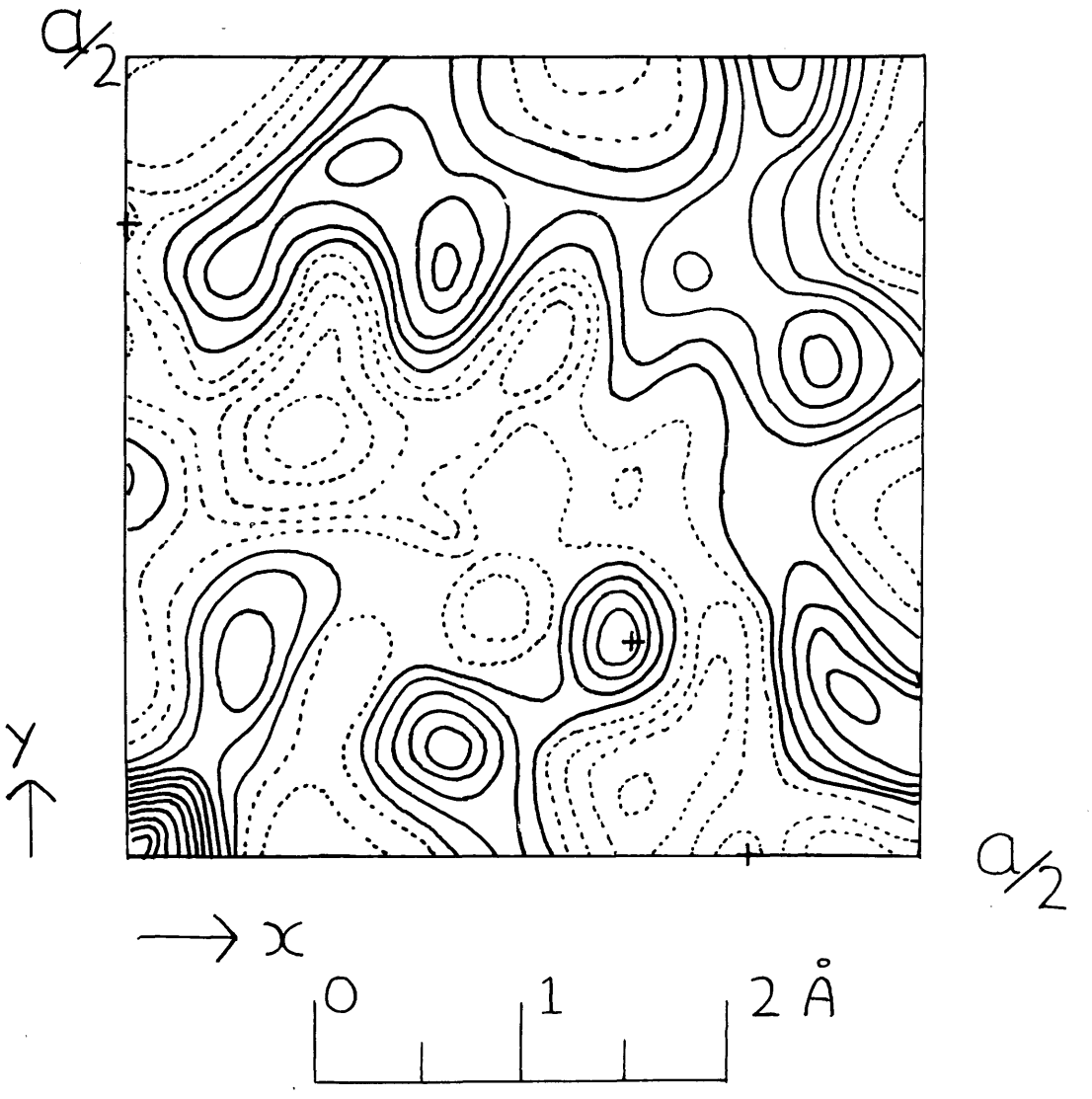


Fig.II. A difference Fourier section (x,y,0), through the plane of the molecule of dinitrogen tetroxide. The contours are drawn at intervals of 0.1 electrons/Å^3, the negative contours being shown by the discontinuous lines.

TABLE I.

The Molecular Dimensions of Dinitrogen Tetroxide.

	Broadley and Robertson	Smith and Hedberg	Present Work
N - N Bond	1.64 ± 0.03 Å	1.75 Å	1.66 ± 0.03
N - O Bond	1.17 ± 0.03 Å	1.18 Å	1.16 ± 0.02
O - O (Non-bonded distance)	2.09 ± 0.03 Å	2.17 Å	2.09 ± 0.02
O - O (Non-bonded distance)		2.68 Å	2.65 ± 0.03
O - N - O	126° ± 1°	133.7°	129° ± 1.5°

TABLE II.

	x/a	y/b	z/c	b_{11}	b_{22}	b_{33}	$b_{12}(\times 10^5)$
Nitrogen	0.3952	-	-	1051	1203	1037	-
Oxygen	0.3295	0.1546	-	1900	1456	1354	1918

TABLE III.

Observed and Calculated Structure Factors for Dinitrogen Tetroxide.

H	K	L	F_o	F_c	H	K	L	F_o	F_c
0	0	2	68.88	+67.64	0	4	4	30.16	-33.24
0	0	4	< 6.76	+ 3.68	0	4	6	11.44	-13.84
0	0	6	45.12	+49.04	0	4	8	14.52	-19.12
0	0	8	21.08	+24.96	0	5	1	21.08	-22.16
0	0	10	11.44	+15.24	0	5	3	42.72	+36.20
0	1	1	23.48	-20.96	0	5	5	12.44	+10.44
0	1	3	89.60	+85.80	0	5	7	8.12	-14.32
0	1	5	23.44	+18.80	0	6	2	< 9.10	- 1.28
0	1	7	< 9.58	+ 0.76	0	6	4	12.44	-10.56
0	1	9	< 8.14	+ 7.76	0	6	6	13.40	+12.56
0	2	2	4.76	- 8.40	0	7	1	< 9.66	+ 4.88
0	2	4	8.12	+ 4.80	0	7	3	25.92	+31.68
0	2	6	19.68	+15.16	0	7	5	8.12	+ 9.32
0	2	8	< 9.09	- 2.80	0	7	7	9.52	+ 3.64
0	3	1	16.76	-17.76	0	8	2	14.36	+10.16
0	3	3	< 6.68	+ 3.52	0	8	4	< 7.74	+10.60
0	3	5	11.48	- 8.20	0	8	6	10.00	+13.36
0	3	7	< 9.67	+ 5.32	0	9	1	< 8.12	- 1.68
0	3	9	< 5.72	+ 1.88	0	9	3	< 5.72	+ 4.60
0	4	2	35.48	-35.92	1	1	2	50.04	-44.44

- Cont'd -

TABLE III. - Cont'd -

Observed and Calculated Structure Factors for Dinitrogen Tetroxide.

H	K	L	F_o	F_c	H	K	L	F_o	F_c
1	2	3	37.12	+37.24	2	4	6	< 6.20	- 6.68
1	3	2	< 4.03	- 4.76	2	5	3	18.24	+22.16
1	3	4	27.36	-24.42	2	5	7	< 4.99	+ 4.72
1	4	3	23.20	+22.80	2	6	4	15.84	-15.68
1	4	5	6.16	- 8.08	2	7	5	< 4.99	- 0.56
1	5	4	8.64	+ 3.52	3	3	6	10.84	- 8.80
1	5	6	< 6.20	+ 5.80	3	4	7	11.48	-12.48
1	6	5	11.80	-11.44	3	5	8	< 3.06	+ 0.76
1	6	7	< 4.35	- 0.52	3	7	4	13.64	+10.76
1	7	6	7.76	- 7.80	3	8	5	21.04	+16.44
2	2	4	12.68	+12.68	4	4	8	5.56	+ 1.28
2	3	5	13.24	+10.88					

A P P E N D I X III.

The Crystal Structures of Furan Tetracarboxylic Acid and its Salts.

Cocker, Davis, McMurry and Start (1959) have investigated the properties of furan tetracarboxylic acid (Fig.I) and its mono Potassium salt.

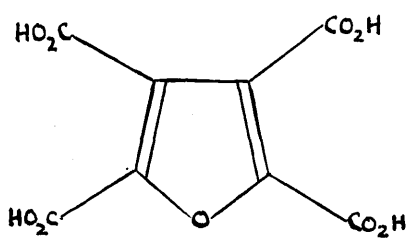


Fig.I.

From the infra-red spectra of these compounds, they predict a high degree of hydrogen bonding in both compounds. The infra-red spectra of the Potassium salt indicates that it has a different type of hydrogen bonding from that found in the maleate ion (Cardwell, Dunitz and Orgel (1953)) and (Darlow and Cochran, 1961). Professor Cocker has kindly provided samples of both compounds for detailed X-ray analysis.

The preparation of crystals of furan tetracarboxylic acid suitable for X-ray analysis has proved impossible. The potassium salt, however, crystallises in the form of fine needles. A mono Rubidium salt of furan

tetracarboxylic acid has also been prepared and it has a similar crystal form to that of the Potassium salt.

The unit cell dimensions, space group, and number of molecules in the cell has been determined for both compounds. The results are given in Table I. From these results, a strong degree of isomorphism is indicated, although the analytical data suggest that the number of molecules of water of crystallisation is different for the two molecules. A further criterion for a strong structural relationship between the salts is the close resemblance of the (hOℓ) zone of reflexions for both compounds.

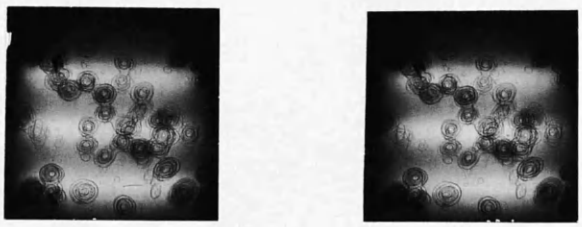
It is hoped to continue this analysis, using the Rubidium atom to determine the signs of the reflexions for that salt, and hence to proceed to work on the Potassium salt, where more accurate molecular dimensions could be obtained.

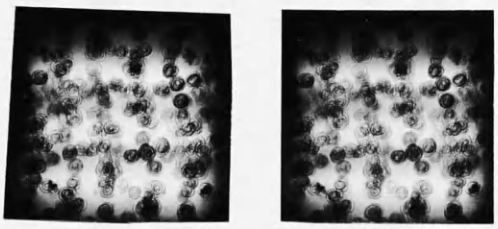
TABLE I.

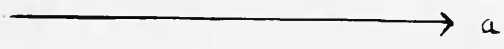
	Potassium Salt	Rubidium Salt
Formula	$C_8H_3O_9K.2H_2O$	$C_8H_3O_9Rb.\frac{1}{2}H_2O$
M	308	337.5
d (meas.)	2.07 gm./cc.	2.20 gm./cc.
d (calc.)	2.14 gm./cc.	2.26 gm./cc.
n	4	4
a	9.61 ± 0.06 Å	9.70 ± 0.05 Å
b	6.30 ± 0.04 Å	6.38 ± 0.04 Å
c	17.56 ± 0.08 Å	17.70 ± 0.10 Å
β	$115^\circ\ 30'$	$115^\circ\ 40'$
V	957.8 $Å^3$	990.4 $Å^3$
Absent Spectra	h0l when l is odd	
	0k0 when k is odd	
Space Group	$P2_1/c$ (C_{2h}^5)	$P2_1/c$ (C_{2h}^5)
F(000)	648	660

A P P E N D I X IV.

Stereoscopic pairs of photographs of the final three-dimensional Fourier maps, drawn up on glass, are shown for clerodin bromolactone (I) and atrovenetin trimethyl ether ferrichloride (II).







In (I), the region of the photograph covers one molecule, which is drawn representing the true

absolute configuration. In (II), the Fourier map contains several molecules, and it is hoped that some idea of the packing is conveyed. The plane of the paper corresponds to the pseudo glide plane in the direction of the a-axis, which is marked. (cf. Fig.IV in atrovenetin section.)

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